***United States Court of Appeals***

***for the Second Circuit***

# APPENDIX

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# NO. 74-2284 et al.

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NOS. 74-2284, 74-2286, 74-2308, 74-2450, 74-2449

JOINT APPENDIX TO THE BRIEFS

VOLUME I

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IN THE UNITED STATES COURT OF APPEALS
FOR THE SECOND CIRCUIT

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THE SOCIETY OF THE PLASTICS INDUSTRY, INC.,

HOOKER CHEMICALS & PLASTICS CORP.,

UNION CARBIDE CORPORATION,

TENNECO CHEMICALS, INC.

and

AIR PRODUCTS AND CHEMICALS, INC.,

Petitioners,

v.

OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION,
UNITED STATES DEPARTMENT OF LABOR;
PETER J. BRENNAN, SECRETARY, DEPARTMENT OF LABOR;
and JOHN H. STENDER, ASSISTANT SECRETARY
FOR OCCUPATIONAL SAFETY AND HEALTH,

Respondents.

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On Petition For Review Of An Order Of
The Occupational Safety and Health Administration,
United States Department of Labor

UNITED STATES COURT OF APPEALS
FILED
DEC 10 1974
A. DANIEL FUSARO, CLERK
SECOND CIRCUIT

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Products and Chemicals, Inc.

November 12, 1974

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## Title 29—Labor

## CHAPTER XVII—OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION, DEPARTMENT OF LABOR

## PART 1910—OCCUPATIONAL SAFETY AND HEALTH STANDARDS

### Standard for Exposure to Vinyl Chloride

Pursuant to sections 6(b), 6(c), and 8(c) of the Occupational Safety and Health Act of 1970 (84 Stat. 1593, 1596, 1599; 29 U.S.C. 655, 657) Secretary of Labor's Order No. 12–71 (36 FR 8754) and 29 CFR Part 1911, § 1910.93 of Part 1910 of Title 29, Code of Federal Regulations is hereby amended in the manner set forth below, in order to provide an Occupational Safety and Health standard dealing with the exposure of employees to vinyl chloride.

I. *Background*—(1) *Vinyl chloride.* Vinyl chloride (chloroethene), Chemical Abstracts Service Registry No. 75014, is a synthetic organic chemical made from ethylene or acetylene and chlorine by any of several processes. It is the parent compound of a series of thermoplastic resin polymers and copolymers which are widely used for containers, wrapping film, electrical insulation, pipe, conduit, and a variety of other industrial and consumer products. Vinyl chloride has been made commercially in this country since 1939, and present production is in excess of seven billion pounds per year. The vinyl chloride industry divides into three segments: monomer production, polymer production, and fabrication. Production of the monomer is a large-scale continuous process, involving only a few firms. There are comparatively few employees in this segment of the industry, because the processes lend themselves to automation.

Vinyl chloride (VC) is used primarily in the production of polyvinyl chloride (PVC), a resin which is produced through batch processing. The conversion of the VC monomer into a polymer or copolymer is an incomplete process, i.e., not all of the monomer is reacted.

PVC is fabricated by a variety of techniques, including extrusion, injection molding and calendering, to form a finished product that needs no further chemical handling. The vast majority of employees involved in the VC industry are employed by fabrication firms. Such firms range in size from those with few employees and simple equipment to large plants involving many employees and considerable capital.

Vinyl chloride (VC), a gas at ambient temperature and pressure, is a chlorinated hydrocarbon, which heretofore has been regarded as having moderate liver toxicity. The initial standard, contained in Table G–1 of 1910.93, established a ceiling value of 500 parts of VC per million parts of air.

(2) *The emergency temporary standard.* On January 22, 1974, the Occupational Safety and Health Administration (OSHA) was informed by the National Institute for Occupational Safety and Health (NIOSH) that the B. F. Goodrich Chemical Company had reported that deaths of several of its employees from a rare liver cancer (angiosarcoma) may have been occupationally related. As a result of this notification and after consultation with NIOSH, and a joint inspection of the B. F. Goodrich plant by OSHA, NIOSH and the Kentucky Department of Labor, a fact-finding hearing was announced on January 30, 1974 (39 FR 3874) and held on February 15, 1974.

Information obtained from this hearing, particularly the preliminary reports of experiments conducted by Professor Cesare Maltoni of the Instituto di Oncologia, Bologna, Italy, demonstrated that vinyl chloride induced angiosarcoma in rats at levels as low as 250 ppm, and in other species at higher levels. Experiments performed at lower levels of exposure were not completed at that time. Other testimony from medical witnesses and NIOSH, and the results of autopsies, led to the conclusion that the Goodrich workers had angiosarcoma of the liver and that VC probably was the causal agent in the angiosarcomas observed.

In post hearing comments, additional angiosarcoma deaths were reported among workers who had been exposed to VC in plants operated by Union Carbide Corporation, Firestone Plastics Corporation and Goodyear Tire & Rubber Company.

On the basis of all information available at that time, and the fact that employees were being exposed at levels around the experimentally observed effect level of 250 ppm, an emergency temporary standard (ETS) was promulgated on April 5, 1974 (39 FR 12341) pursuant to section 6(c) of the Act, as 29 CFR 1910.93q.

This standard reduced the permissible exposure level from a ceiling of 500 ppm to a 50 ppm ceiling, and established other requirements, including, for example, monitoring and respiratory protection. It was expressly recognized that this standard limiting exposures to a 50 ppm ceiling was a tentative, interim standard, and that the whole question of exposure to VC would be considered more fully in the light of additional information, especially the results of experiments which were known to be underway at that time.

On April 15, 1974, information and data were presented to representatives of OSHA, NIOSH, and the Environmental Protection Agency by the Industrial Bio-Test Laboratories, Northbrook, Illinois, concerning results of animal exposure studies with VC. These studies were sponsored by the Manufacturing Chemists Association. Although only preliminary in nature at that time, these results revealed that 2 out of 200 mice exposed to VC concentrations of 50 ppm for 7 hours a day, five days a week, for approximately 7 months, had developed angiosarcoma of the liver.

(3) *The proposed permanent standard.* Based on the demonstrated evidence of VC's carcinogenicity in three animal species (rats, mice and hamsters), and the substantial probability that VC had been the causal agent in the cases of liver angiosarcoma found in workers both here and abroad, OSHA proposed to revise 1910.93q and published a comprehensive proposal (39 FR 16896) on May 10, 1974, to protect employees from hazards of exposure to VC. The proposal called for limitation of employee exposure to VC to "no detectable level," as measured by a sampling and analytical method sensitive to 1 ppm, with an accuracy of 1 ppm ± 50 percent. The proposal also called for the establishment of regulated areas and limited access to such areas to authorized persons. A requirement for monitoring of employee exposures was proposed, along with engineering and work practice controls to be implemented when exposures over the detectable limit were measured.

Respiratory protection would have been required while engineering and work practice controls were being implemented or where exposures exceeded the permissible limit even after feasible engineering controls were instituted.

In addition, the proposed standard included requirements for medical surveillance, protective clothing, emergency procedures, training, specific protection during maintenance and decontamination operations, transportation loading and unloading operations and record-keeping.

(4) *Hearing on the proposal.* The proposal, as published on May 10, 1974, allowed 30 days for interested parties to submit written comments and to request an informal rulemaking hearing. Informal contacts with OSHA staff and early responses indicated that the subject was of great interest and importance to many persons. Because of the limited time available before expiration of the six month period provided in section 6(c)(3) of the Act for promulgation of a final standard, it was decided to hold a hearing as soon as possible. Accordingly, on May 24, 1974, a notice of a hearing was published (39 FR 18303), setting a hearing date of June 25, 1974. The hearing was conducted from June 25 through June 28, and again from July 8, through July 11, before Administrative Law Judge Gordon J. Myatt. All participants were given the opportunity to present testimony and to cross-examine other witnesses. Persons participating in the hearing were given until August 23, 1974, to file additional posthearing comments, including various items of information which were requested during the examination of witnesses.

(5) *Economic and technical impact study.* During the hearing, OSHA determined that additional facts would be needed to determine the practicality of certain aspects of the proposed standard. Accordingly, OSHA contacted an independent consultant, Foster D. Snell Corporation, to conduct studies of the feasibility of compliance at various exposure levels, including those proposed by OSHA and others advanced by industry spokesmen. Snell was also commissioned to collect information regarding the economic costs of compliance. This action was announced at the close of the hearing, and Judge Myatt further announced that the record would be kept

open for a period of time beyond August 23, to allow interested persons to comment in writing on the study. On August 26, 1974, OSHA announced that the preliminary study was available and that comments were to be submitted no later than September 6, 1974 (39 FR 30844). On September 13, 1974, OSHA invited comments on both the preliminary and the final study, which was to be received on or before September 25, 1974 (39 FR 33009).

(6) *Environmental impact statements.* A notice of intent to file an environmental impact statement assessing the impact of a proposed standard on occupational exposure to VC was published in the FEDERAL REGISTER on April 24, 1974 (39 FR 14522). The notice invited any person having information or data on the environmental impact to submit it to OSHA by May 17, 1974. On June 12, 1974, a draft environmental impact statement was prepared and circulated to all interested persons. Ten copies were forwarded to the Council of Environmental Quality (CEQ), which published a notice of its filing and availability in the FEDERAL REGISTER on June 25, 1974 (39 FR 22975). A 45 day period was allowed for the submission of comments on the draft statement. On September 5, 1974, the final environmental impact statement was prepared and a copy of it and all substantive comments were sent to appropriate governmental agencies, private organizations, and other interested persons. CEQ published a notice of availability for the final statement on September 6, 1974 (39 FR 32350). The submission of comment was invited until September 25, 1974. The final statement and all significant comments have been carefully considered in arriving at the final standard on occupational exposure to VC.

(7) *The record.* The record in this proceeding is one of the most exhaustive ever relied upon by OSHA. It consists of pre and post-hearing comments and testimony received at both factfinding and rulemaking hearings, the studies and inspections conducted by OSHA personnel, the environmental impact statements, the economic and technical impact studies, and all other relevant information. In all, over 600 written comments have been received, with more than 200 separate oral and written submissions made with regard to the two hearings. The record itself exceeds 4,000 pages. Employers, employees, labor unions, public health groups, independent experts, physicians, research scientists, and specialists in many fields have been invited to submit information and have made their views, knowledge and experience available to OSHA. The entire record encompassing these submissions was thoroughly reviewed and evaluated in reaching the determinations set forth below.

II. *Findings regarding carcinogenicity, exposure levels and feasibility*—(1) *Carcinogenicity of vinyl chloride.* The carcinogenicity of vinyl chloride for three animal species (rat, mouse, hamster) has been documented on the record by the studies of Maltoni and Bio-Test Laboratories. Moreover, Maltoni's investigations have demonstrated a dose-dependent relationship for induction of tumors (i.e., more tumors occur at higher exposure levels), including angiosarcoma of the liver, in rats. The investigations of Industrial Bio-Test Laboratories have demonstrated a similar relationship for both rats and mice. These investigators have induced angiosarcoma of the liver in rats and mice at exposure concentrations of 50 ppm, and in hamsters at higher concentrations of exposure. Additional tumors involving other organs, including the kidneys, lungs, and skin of exposed animals, were also observed in frequencies much in excess of control animals. The incidence of tumors in mice in the Industrial Bio-Test Laboratories investigations is particularly pertinent. Of 200 mice (100 males, 100 females) exposed to 50 ppm of vinyl chloride by inhalation for eleven months, 100 died. Sixty-four animals died without gross postmortem pathologic examination being performed. Of the 36 remaining animals for which a gross postmortem pathologic examination was performed, 13 (36 percent) were found with liver tumors (including angiosarcomas), 21 (58 percent) with lung tumors, 9 (25 percent) with skin tumors, and one with a kidney tumor.

According to the 1970 report by the Surgeon General's Ad-Hoc Committee on the Evaluation of Low Levels of Environmental Chemical Carcinogens, the finding of cancer in two or more animal species may be extrapolated to indicate a carcinogenic hazard to humans. Here, such a finding was made in three species that were exposed to VC by inhalation—a route comparable to employee exposure. In addition, there were at least 13 confirmed cases of angiosarcoma of the liver among employees exposed to VC, a particularly significant number in view of the extreme rarity of this cancer in the U.S. adult male population (testimony of Dr. Marcus Key, Director of NIOSH, at the rulemaking hearing).

The findings of angiosarcoma of the liver in both experimental animals and exposed employees is compelling evidence that exposure of humans to vinyl chloride induces this tumor. Industry spokesmen, at the hearing, conceded that VC is carcinogenic for humans (e.g. testimony of Dr. McBurney, Rulemaking hearing, 1041). Accordingly, it is concluded that VC must be regarded as a human carcinogen, and the probable causal agent of angiosarcoma of the liver, and that exposure of employees to VC must be controlled.

Additional evidence of tumor induction in a variety of other organs, including lung, kidney, brain and skin, as well as non-malignant alterations, such as fibrosis and connective tissue deterioration, indicates additional oncogenic and toxicologic properties of vinyl chloride, which must be considered in establishing control regulations. (See testimony and results of studies by Bio-Test Laboratories, Tabershaw-Cooper, Maltoni, NIOSH, and Selikoff.)

(2) *Exposure limits.* Upon finding that exposure of employees to vinyl chloride may create a carcinogenic hazard, the amount of exposure which is hazardous must be determined. The Surgeon General's Ad Hoc Committee referred to above concluded that safe exposure levels for carcinogenic substances cannot be scientifically determined. This position is supported by the testimony of NIOSH at the hearing, its recommendations for a standard of no detectable level, and by the testimony of expert witnesses from the National Cancer Institute.

Several witnesses and persons who submitted comments have taken a contrary view and have suggested that man is less sensitive to biologic aberrations induced by vinyl chloride exposure than experimental animals. Proponents of this position have argued that if humans were as sensitive as rodents, an "epidemic" of cancer resulting from VC exposures should have already been discovered among employees. They also argue that the employees in whom tumors have been observed are those who have considerable employment experience as polymerization reactor cleaners. Because it is generally agreed that reactor cleaning involved high exposures to vinyl chloride in years past, it is argued that the lower levels currently found in the workplace have not induced cancer and are therefore safe. We reject this argument.

The fact that approximately three-quarters of those employees with the longest exposure to VC (greater than 20 years since initial exposure) have not yet been located, makes it impossible to determine the actual number of affected employees. The cases of liver tumors observed to date have an average latency period, since initial exposure, of approximately 20 years. If it is assumed that induction of angiosarcoma is a dose-related phenomenon, and if employees engaged in cleaning reactors did, in fact, receive larger doses of vinyl chloride, it would be expected that such tumors would be observed earlier for this employee population. For this reason, the significance of presumed lower doses cannot be accurately assessed until a longer period of time has passed, as a longer induction period would be expected.

Initiation of exposure to chemical carcinogens and induction of cancer are not necessarily synchronous events. Because of the physiologic complexities involved with carcinogenesis, induction of tumors does not occur in all employees with similar exposure histories. For example, Dr. Schneiderman of the National Cancer Institute emphasized during his testimony that only about a fifth of longer-term heavy smokers develop lung cancer. Accordingly, the industry contention that exposure levels have been dramatically reduced since the 1940's is not reliable evidence that current levels of exposure are safe.

Some industry spokesmen also suggested that the apparent nonrandom distribution of observed cancer in employees may indicate an exposure threshold for tumor induction, based on variations in the workplace design or practice and resultant employee exposures

(testimony and questioning by Tenneco Chemicals, Inc.). It has also been emphasized that in only 3 of 8 polymerization plants where employees have been exposed to VC for more than 20 years have any employees developed angiosarcoma of the liver. This argument is very similar to that raised concerning variability of past employee exposure. Although geographic and workpractice differences may ultimately be demonstrated to be factors in distribution of angiosarcoma, sufficient information is unavailable to exclude from consideration of risk those employees in workplaces for which cases of angiosarcoma have not been observed.

It has also been suggested that the absence of cancer in a population of 335 Dow Chemical Company polymerization employees monitored over a period of 7 years, indicates that exposure to vinyl chloride at concentrations of less than 200 ppm is safe. (See study by Dr. Cook, submitted at the hearing by Dow Chemical Company.) However, the group surveyed did not include all workers who had been exposed, and the missing employees included many who had the longer term (over 20 years) exposures. Moreover, the statistically insignificant size of the sample population decreases the possibility that tumors would be observed.

Dow also presented preliminary data in testimony at the hearing on the possible metabolic pathways of VC. The hypothesis presented was that VC may exert its carcinogenic effect by a metabolite, and that the metabolite is produced only when VC is metabolized by a secondary metabolic pathway operating only when enzymes regulating the primary pathway are saturated, as would be the result at higher exposures. The preliminary data indicated the possibility of an additional pathway for metabolism of VC in rats exposed to concentrations of VC in excess of 220 ppm. However, the occurrence of angiosarcoma in both rats and mice at VC exposure concentrations of 50 ppm indicates that if a metabolite of VC is the ultimate carcinogen, then it must be generated at lower exposure concentrations in these species. Although this research may be helpful to the thorough understanding of the carcinogenicity of VC, it appears that it does not yet offer evidence which can assist in determination of safe exposure concentrations for employees, or even that such safe exposures exist.

A number of witnesses representing employers have stressed that there is no evidence of cancer, either in employees or experimental animals, at exposure concentrations of VC less than 50 ppm. (See e.g., testimony of Firestone, Tenneco Chemicals.) The conclusion of these witnesses was that no decision can be made concerning risk of exposure to VC at concentrations less than 50 ppm.

On the other hand, the testimony of most expert witnesses, including some industry biomedical experts, stated that quantification of a safe exposure concentration is not possible with the present state of scientific knowledge. (See e.g., testimony of Selikoff, Firestone, NCI, and NIOSH.)

In our view, the demonstration of cancer induction in humans at a particular level is not a prerequisite to a determination that a substance represents a cancer hazard for humans at that level. It would be imprudent to assume man to be less sensitive to VC exposure than experimental animals in the absence of conclusive evidence. It would also be unfounded to assume that animals will not develop tumors when exposed at concentrations of VC of less than 50 ppm. Should a sufficiently large number of experimental animals be exposed to VC at concentrations of less than 50 ppm, Schneiderman said that it would be expected that some would develop VC induced tumors.

(3) *Feasibility.* There is virtually no dispute that most, if not all, fabricators are currently capable of reaching exposure levels of 1 ppm through engineering controls. These employers employ well over 95 percent of all employees exposed to VC. Indeed, several fabricators are already operating at this level (see SPI testimony). However, industry spokesmen have universally claimed that it is infeasible for the VC and the PVC industries to remain below 1 ppm consistently, using engineering controls. In addition, the Snell study on technical feasibility concluded that a 1 ppm ceiling is not feasible for the VC and PVC industries with present technology, but that the VC industry could currently attain lower exposure levels than the PVC industry. Labor union spokesmen and the Health Research Group, Inc., however, have suggested that such a level is attainable.

Since there is no actual evidence that any of the VC or PVC manufacturers have already attained a 1 ppm level or in fact instituted all available engineering and work practice controls, any estimate as to the lowest feasible level attainable must necessarily involve subjective judgment. Likewise, the projections of industry, labor, and others concerning feasibility are essentially conjectural. Indeed, as Firestone has suggested, it is not possible to accurately predict the degree of improvement to be obtained from engineering changes until such changes are actually implemented.

We agree that the PVC and VC establishments will not be able to attain a 1 ppm TWA level for all job classifications in the near future. We do believe, however, that they will, in time, be able to attain levels of 1 ppm TWA for most job classifications most of the time. It is apparent that reaching such levels may require some new technology and work practices. It may also be necessary to utilize technology presently used in other industries. In any event, the VC and PVC industries have already made great strides in reducing exposure levels. (See testimony of Dow Chemical Co., TR 973). For example, B. F. Goodrich testified (TR 1120) that it has reduced average exposure levels in several PVC plants from 35–40 ppm early this year to 12–13 ppm at the time of the hearing. We are confident that industry will continue to do so.

(4) *Conclusions.* The conclusions below are based on a thorough review and evaluation of all the evidence submitted. Where decisions can be based on record evidence, this has been done. Where, however, factual certainties are lacking or where the facts alone do not provide an answer, policy judgments have been made.

There is little dispute that VC is carcinogenic to man and we so conclude. However, the precise level of exposure which poses a hazard and the question of whether a "safe" exposure level exists, cannot be definitively answered on the record. Nor is it clear to what extent exposures can be feasibly reduced. We cannot wait until indisputable answers to these questions are available, because lives of employees are at stake. Therefore, we have had to exercise our best judgment on the basis of the best available evidence. These judgments have required a balancing process, in which the overriding consideration has been the protection of employees, even those who may have regular exposures to VC throughout their working lives.

Based on the available evidence and in view of the above considerations, including feasibility, we believe that employee exposures to VC must be reduced to a 1 ppm time-weighted average (TWA). We also believe that PVC and VC establishments will, in time, be able to attain that level through engineering controls, and that fabricators can do so in the immediate future.

In addition to the TWA requirement, we have established a 5 ppm ceiling (averaged over a 15-minute period) in order to prevent exposure of employees to unacceptable high excursions. From an operation standpoint, this ceiling level is realistic because minor excursions up to the ceiling level are likely to occur on a regular basis.

III. *The final standard*—(1) *Scope and application.* Both the ETS and the proposal would apply the standard to the entire VC industry, including manufacturers of VC and PVC and fabricators, but excluding employers handling or using fabricated products made from VC.

There is no dispute that a standard is required for the monomer and polymer industries. However, the Society of Plastics Industry (SPI) and various fabricators (see testimony of Goodyear, General Cable, etc.) recommended that fabricators be excluded from the standard, or that a separate requirement be established for them because many of them were already at or below the proposed ceiling level.

The record evidence establishes that at least some employees in the fabricating industry are exposed in excess of the permissible control limits (See NIOSH testimony, TR 106; Robintech TR 642). In these circumstances, we believe that it is imprudent to grant a blanket exemption for all fabricators. Therefore, the final standard is applicable to the fabrication industry, as well as the monomer

and polymer industries. Employers who, in fact, are substantially below the exposure limit will be subjected to only minimal burdens by virtue of the "action level" to be discussed below.

Where employers in the fabricating industry have exposures approaching the permissible limit, they will appropriately be subject to the standard. Employers handling or using fabricated products made of PVC were not included in the ETS or the proposal and are excluded from the final standard. This conclusion is based on the absence of adequate evidence of exposure to VC in these operations. The final standard clarifies the exemption by defining a fabricated product as a product made wholly or partly from PVC which does not require further processing at temperatures, and for times, sufficient to cause mass melting of the PVC. SPI and others (cf. TR. 344) requested that PVC resins with less than 0.1 percent residual monomer be exempted from the regulation now, and that the exemption level be reduced to 0.01 percent in three years. SPI suggested that the exemption of materials with less than 0.1 percent of 14 carcinogens from 29 CFR 1910.93p (39 FR 3756) was an appropriate precedent. The cases are not comparable, because no attempt had been made to set air concentration limits for the 14 carcinogens. The record did not include information that reliable monitoring and measuring techniques were available. Moreover, the exemption did not exempt airborne traces of carcinogens. The administrative cutoff was provided to avoid regulation of materials about which there was no health hazard information, and which would have broadly extended the application of the regulation beyond the record. Herein, no information was presented to show safe concentration results from the use of resins with specific levels. Indeed, the proposal to change the level later, when improved technology would permit such reduction, would seem to indicate that SPI has doubts about the safety of 0.1 percent residue level. Diamond Shamrock (Exhibit 142) testified that there is no direct relation. They indicate that the airborne concentration is more related to the physical form of the resin and the ventilation provided. Also, monitoring data from industry (cf. Exhibits 131, 168, 170) and OSHA (Exhibit 151) indicate that levels in excess of 1 ppm may be found in fabrication operations. In view of these facts and of the opportunity for employers to discontinue many duties upon a showing of no exposures above the action level, it does not appear that any residue exemption is either justified or necessary at this time. This course also agrees with a number of industry proposals (cf. TR 660).

SPI (TR 345), among others, asked that compounded PVC pellets be exempted from the standard on the grounds that the pellets had too low a residue to cause harmful or measurable emissions. While it appears that PVC pellets would have a lower residue level than virgin PVC, the fact that the pellets must be heated to a molten mass at the same temperature as PVC, for further processing, indicates that a potential for release of the residue still exists. It appears that the exemption of fabricated products should be limited to just those items which will not undergo such mass heating. Further, the opportunity to demonstrate that exposures are below the action level, and thus, discontinue many duties of the standard, provides a more positive control and an adequate relief.

(2) *Permissible exposure limit.* The standard sets an exposure limit of 1 ppm averaged over any 8 hour period, and a ceiling of 5 ppm averaged over any period not exceeding 15 minutes.

As more fully discussed above, this limit is based on an evaluation of the best available evidence and on a judgment that the health and safety of employees must be protected to the fullest extent feasible. In view of the fact that release of VC in the VC and PVC manufacturing processes are variable, the 1 ppm ceiling level provided in the proposal would require maintenance of an average level significantly more difficult to attain through feasible engineering controls. Therefore, the exposure limit prescribed in the proposal has been rejected.

(3) *Action level.* The final standard, unlike the ETS and the proposal, provides for an "action level" of 0.5 ppm TWA, one-half of the permissible exposure limit. The purpose of the action level is to minimize the impact of the standard on the employers who have attained exposure levels well below the permissible limit. Thus, where the results of monitoring under paragraphs (d)(1) or (d)(2) demonstrate that no employee is exposed in excess of 0.5 ppm TWA, employers may, in effect, be exempted from some provisions of the standard. For example, fabricators who are below the action level are not required to provide medical surveillance or to monitor again, unless the employer has reason to suspect that any employee is exposed in excess of the action level. In our judgment, exposures below the action level do not present a sufficient hazard to warrant application of the entire standard to the many employers who are or will be below that level.

(4) *Monitoring.* The final standard, like the proposal, requires that individual employee exposure levels be determined. This may be accomplished by personal or area monitoring. Some witnesses and persons who submitted comments did not understand the meaning of the term "95 percent confidence level" in the proposal. Essentially it means that the employer is required to take a sufficient number of measurements so that the results obtained are statistically valid. We have modified the proposal to establish accuracy range requirements for various measurement levels. These ranges are narrow enough to ensure that a determination of compliance can be made, and broad enough to allow the application of a variety of technologies.

All covered employers are required to conduct initial monitoring. Where monitoring and measuring results are at or below the action level, no further monitoring is required unless the employer has reason to suspect that any employee is exposed in excess of the action level, or unless changes have been made in production, process, control, type of resin, etc.

Where the exposure level, without regard to respirators, exceeds the permissible levels, monitoring must be conducted at least monthly. Where exposures are less than the permissible levels, but greater than the action level, monitoring must occur at least quarterly.

(5) *Methods of compliance.* The standard, like the proposal, requires that employers immediately institute feasible engineering and work practice controls to reduce exposures to at or below the permissible exposure limit.

Where feasible engineering and work practice controls will reduce exposures below the permissible levels, they must be instituted. Where such controls will not reduce exposures below the permissible level, they must nonetheless be implemented to reduce exposures to the lowest practicable level, and be supplemented by the use of respirators to provide the necessary protection. Thereupon, a continuing program of engineering and work practice controls must be instituted to reduce exposures to the lowest practicable level. When exposures are at or below the permissible exposure limits, the program may be discontinued.

In addition, a plan for achieving control by engineering and work practice methods must be drawn up and be made available, upon request, to representatives of OSHA and NIOSH.

We recognize that many employers covered by the standard can not currently achieve compliance with the permissible exposure limit solely by the use of feasible engineering and work practice controls. The record also reflects broad generic distinctions between the compliance capabilities of the VC and PVC industries. Some industry spokesmen, including S[illegible] (TR. 358-362), recommended that a schedule of different permissile exposure limits and compliance dates be established for the VC and PVC segments of the industry.

This view assumes that the ability and the time required to feasibly reach increasingly lower control levels is similar within each industry, but differs markedly between industries. While the record does suggest that such differences do exist between industries, as noted above, it is clear that intra-industry differences also exist. Thus, the ability and time required by each employer to attain lower control levels may depend upon such factors as the climate in which the plant is located, the age of equipment, the size of reactors, or the type of resin manufactured or used. (Snell study, Firestone testimony, etc.)

Monitoring data also tends to support such intra-industry variations. (See, e.g. Dow, Firestone, Tenneco.)

As noted above, the standard requires all employers to institute feasible engineering controls to the fullest extent and to continue to improve and apply engi-

neering controls until full compliance is achieved.

We have not established any deadlines for full compliance through engineering controls because we are presently unable to determine when it will be feasible for most establishments to reduce exposure levels to the permissible level.

We also believe that the requirement that each employer reduce airborne concentrations to the permissible level, or to the lowest level feasible as soon as practicable will provide for inter-industry and intra-industry technological differences which do exist, and will avoid the setting of separate industry standards on the basis of the general situation and conditions in each industry.

(6) *Regulated areas.* The proposed standard would have required that regulated areas be established, that access be limited to authorized employees, and that daily rosters or summaries of those entering be kept for at least 20 years. In objection to these requirements, it was asserted that such control of access was not necessary from a health standpoint. Secondly, it was claimed that these controls would interfere with operations by preventing access of needed employees or non-employees, such as contractors, truck drivers, customers and consultants.

The purpose of establishing regulated areas in the proposal was to limit the risk of exposure to as few employees as possible. This concern is still paramount, and thus the limited access feature remains. The final standard amends the proposal slightly to allow "authorized persons" to enter regulated areas. This change, it is felt, will allow operations to continue without undue interference. The final standard has also increased the length of time daily rosters must be maintained from 20 to 30 years. This change was based largely on epidemiological considerations. (See NIOSH testimony, tr. 119.)

(7) *Respiratory protection.* The final standard, like the proposal, requires the use of respirators where employee exposures exceed the permissible control level. Industry representatives made a number of objections to proposed requirements for respiratory protection. They stated that the "no detectable level" would effectively require continuous wearing of respirators in PVC and VC plants, and that this is not feasible because respirators are cumbersome, present a safety hazard, and employees would not use them.

We would agree that respirators have many drawbacks; the proposal did not contemplate them as a final solution. The record shows that the PVC industry particularly may need several years before plant environmental levels can be reduced so that respirators are necessary only occassionally. However, we cannot agree that respiratory protection should not be required simply because it is inconvenient, may require additional personnel, interferes with production, or may require extensive retraining of employees and restructuring of work practices. We have carefully considered all the objections, and have concluded that if the environmental level is not controlled to the permissible exposure limit, then employees must be afforded respiratory protection.

While exposures in excess of the permissible level do constitute a hazard, we believe that it is necessary to mitigate some of the problems associated with implementing a program of respiratory protection while employees are being fitted and trained in respirator use, and while other adjustments which may be required are implemented. Therefore, until January 1, 1976, where exposures are not in excess of a 25 ppm ceiling, each employer must provide each employee with an appropriate respirator. However, employees whose exposures do not exceed a 25 ppm ceiling, may decline to use the respirator, in which case the employer is not obligated to require its use. During this adjustment period, employees will be trained in the uses, purposes and limitations of respirators, and the hazards of exposure to vinyl chloride. Moreover, each employee will be notified in writing if he has been exposed in excess of the permissible exposure limit.

Where exposures exceed a 25 ppm ceiling, respiratory protection is mandatory in light of our judgment that much greater risks are associated with such exposures.

The provisions in the final standard regarding the selection and use of respiratory protective devices differ from those in the proposal. The descriptions of atmosphere-supplying respirators have been revised to indicate more clearly the types of devices intended, and the maximum permissible concentration level for each device. Moreover, the number of types of atmosphere-supplying devices has been increased.

At the hearing Mr. Edwin C. Hyatt, an OSHA consultant, made suggestions regarding the use of particular respiratory devices. We have concluded that his suggestions are meritorious. Therefore, the provisions for selection of atmosphere-supplying devices follow closely the recommendations contained in his testimony of SPI and B. F. Goodrich) (TR with Hyatt's suggestions. (See e.g. testimony of SPI and B. F. Goodrich) (TR 85 ff) We had originally omitted air-purifying respirators because none had been approved by NIOSH for use against VC, principally because they lacked indicators to signal the expiration of the service life of the sorbent. Hyatt and other witnesses discussed in detail the desirability of being able to use canisters or cartridge air-purifying respirators, provided a sorbent could be shown to effectively absorb vinyl chloride with an adequate service life. Recently, OSHA has received respiratory data from laboratories regarding the effectiveness of commercially available canisters and cartridges for vinyl chloride. These evaluations were conducted separately by NIOSH and by the B. F. Goodrich Company and submitted to OSHA in post-hearing comments. The results indicate that certain presently available canisters and cartridges effectively absorb vinyl chloride at relatively low concentrations. In discussions of these findings with NIOSH, it has indicated that it is willing to consider on an expedited basis the approval of air-purifying respirators for use against VC. Consequently, we have included three types of air-purifying respirators in the list of acceptable units, subject to the approval of such units by NIOSH. The maximum concentration for which each respirator may be used is based upon our evaluation of the data submitted by NIOSH and Goodrich. Because air-purifying respirators do not indicate sorbent exhaustion or breakthrough of VC, and because VC has no inherent warning properties at levels for which these devices are used, strict administrative controls will be required for their use. Such controls include a program to assure timely replacement of canisters or cartridges and an alarm system to alert employees when vinyl chloride concentrations exceed the concentrations allowed for the particular type of respirator in use.

(8) *Hazardous operations.* This is a new section within the final standard. It encompasses essentially the proposal's requirements for maintenance and decontamination but has restated them in terms of performance language to allow greater flexibility for employers to deal with such operations. The intent of the new section is to protect employees engaged in activities that present a risk of exposure to vinyl chloride in excess of the permissible levels. An example would be the cleaning of a filter where resin containing high residual monomer is trapped.

The proposal's requirement for full-body, impervious clothing has been replaced by the direction to use impervious garments suited to the particular situation and probable extent of exposure. Thus, full-body clothing is not always necessary, and is therefore not required where less protection is adequate. Since vessel entry falls within the definition of a hazardous operation, the vessel entry section of the proposal has been deleted from the final standard.

(9) *Emergency situations.* The definition of emergency has been recast in terms of an unexpected massive release. The main objection to the section on emergency situations in the proposal was that, as the term was defined, many ordinary leaks or operations resulting in a small release of vinyl chloride could be considered emergencies. This was not the intent of the proposal. The final standard has been clarified to correct this ambiguity. It should be noted that the written operational plan required by the standard need not be developed for minor excursions above the permissible exposure limit, and that such excursions need not be reported.

(10) *Signs and labels.* The thrust of the signs and labels section is to apprise employees of the cancer and fire hazards. No objections have been raised with respect to informing employees of the fire hazard. However, a number of objections were raised at the hearing and in written submissions to the requirement that the word "cancer" appear on all signs and labels. The principal argu-

ment advanced against its use was that the term "cancer" or "cancer-suspect agent" scares employees and that instead, the message should contain instructions on how to deal with the substance (TR. 347). We believe that a limited form of warning will not suffice. We appreciate the concern of employers with the reaction of their employees. But we consider it imperative that a worker be fully informed, and that he realize the possible risks involved in his occupation. Coupled with the training requirement in the standard, we believe that the signs and labels required will adequately inform employees of the hazard. In addition, such signs will warn unauthorized personnel to keep out of regulated areas.

The proper application of most protective measures requires an amount of training and indoctrination of employees that cannot easily be conveyed on a sign or label. Also, the variety of measures that could be prescribed would result in an unwieldly or excessively detailed legend. Consequently, the required message of signs and labels will not include information on precautions, relevant symptoms, etc. The addition of suitable information by the employer would be permitted, providing it does not detract in any way from the required statement.

The requirement in the proposal for labeling containers of vinyl chloride has been amended by deleting the reference to the possible hazard of violent polymerization. Very little information was developed on this hazard during the standard-setting procedure. It does appear that this hazard is essentially under control and that the fire and carcinogenic hazards at present are the most significant. Since labeling or placarding that is in compliance with the U.S. Department of Transportation regulations (49 CFR Part 173, Subpart H) already warns of the fire hazard, only a statement concerning the carcinogenic hazard need be added to the Department of Transportation labels.

(11) *Medical surveillance.* The principal questions that have been raised regarding medical surveillance are the necessity and efficacy of requiring certain specific serum enzyme determinations (SMA–12 series) and the application of medical examination requirements to the fabrication segments of the industry where employees are exposed to lower levels of VC. The objection has also been raised that the specification of tests and procedures interferes with the application of advances in medical knowledge.

A particular difficulty in considering medical surveillance is that the most commonly discussed lesion, angiosarcoma of the liver, currently cannot be diagnosed until the victim is terminal and, usually, within months of death. Precursor physiologic alterations, which might be reversible, have not yet been directly associated with the lesion. Consequently, there are no specific diagnostic tests which can be prescribed which will determine presence or absence of this tumor at an early stage of development. However, most medical witnesses indicated that the medical tests proposed are currently the only ones available which are useful for medical surveillance (TR 121, Exh. 95, TR 589–591). Consequently, the specific blood tests proposed have been retained as a minimum requirement to assist the examining physician in determining fitness of potential employees for assignment to workplaces involving VC exposure. In addition, alternative medical examinations may be used where the examining physician determines that they are at least as good as those specified by the standard.

The Tabershaw-Cooper study and the various animal experiments suggest that VC may produce a wide spectrum of malignant and non-malignant disorders. The general scope of the required medical examination has, therefore, been broadened to include kidneys, skin, connective tissue, spleen, and pulmonary system, as well as the liver. No additional specific procedures or tests are required, but recommendations have been included in the Appendix to assist the examining physician. Because of the nonspecific nature of the required medical tests, it is not appropriate to prescribe timing, or type of followup tests, or to mandate withdrawal from exposure based solely on results of the tests. Instead, the employer is required to obtain a statement from the examining physician of the employee's suitability for continued exposure, when the examining physician has completed such tests as he considers appropriate. The employer is required to withdraw an employee only when this statement indicates that the employee may be at added risk from continued VC exposure.

As with monitoring, there appears to be no basis for complete exemption of the fabrication industry from the requirement for medical examination. The record does show fabricating establishments with concentrations of VC monitored considerably above the action level. In these instances, medical surveillance of affected employees will provide baseline data for future evaluation of their health, even if both monitoring and medical surveillance are discontinued because improved controls reduce concentrations below the action level. Where exposures are below the action level, the medical surveillance requirements do not generally apply.

(12) *Training.* A separate provision for employee training has been added to the final standard rather than including it within the section on emergency situations as in the proposal. The new paragraph provides for training of employees concerning the carcinogenic hazard of VC, emergency procedures, the need for monitoring and an annual review of the standard. It also provides for training of employees concerning the purpose for, proper use of, and limitations connected with respiratory protection.

(13) *Records and reports.* The provisions for recordkeeping contained in the final standard require the preparation and maintenance of essentially the same information required by the proposal. The major change from the original proposal is the requirement for maintenance of monitoring records and daily roster sheets of authorized persons for 30 years, instead of 20 years. Additionally, the employer is required to maintain medical records for the duration of an employee's employment plus 20 years, or 30 years, whichever is longer. The original proposal called for only 20 years.

This change has been implemented because the latency period for induction of angiosarcoma ranges up to 30 years from initial exposure. Therefore, as a minimum, medical records must be maintained for at least that long. It should be noted that spokesmen for both labor and industry recommended that this change be made.

The reporting requirements are not significantly different from those in the original proposal. However, instead of the requirement for reporting incidents which result in the release of VC into areas where employees may be exposed, the final standard clarifies our original intent by stating that only emergencies must be reported. Also the requirement for filing a detailed, written report within 15 days has been deleted. It has been concluded that submission, within 24 hours, of an initial report that includes facts immediately available, would ordinarily be sufficient. However, if the OSHA Area Director requests further information relevant to the emergency, the employer will be required to furnish such information.

(14) *Deleted portions of the proposal.* The proposal contained provisions requiring that shower facilities and change rooms be provided, and that storage or consumption of food be prohibited in regulated areas. We have deleted these provisions because it is our conclusion they are no longer necessary. Showering facilities are not required because protective clothing, where required by the final standard, should protect employees from skin absorption by direct contact with VC and because there is no reliable evidence that VC vapor is absorbed through the skin. In addition, since we anticipate that most employees will not be wearing protective clothing and that employees who wear protective clothing will change such clothing infrequently, we are not requiring that change rooms be provided.

In addition, we feel that there is inadequate evidence showing that hazardous amounts of VC can be absorbed through ingestion. For this reason, the requirement prohibiting the storage or consumption of food in regulated areas has been deleted.

The proposal also contained provisions on maintentance and decontamination, transportation loading and unloading, and polymer handling operations. These requirements are not mentioned in the final standard because attention to these items is implicit in the requirement that each employer reach the permissable exposure limit or attain the lowest feasible level.

(15) *Effective date.* In order to ensure that affected employers and employees will be informed of the existence of these

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provisions and that employers affected are given an opportunity to familiarize themselves and their employees with the existence of the new requirements, the effective date of the amendment to § 1910.93q will be January 1, 1975. To provide continued protection for employees until that date, the provisions currently contained in § 1910.93q are hereby promulgated, pursuant to section 6(b), 6(c) and 8(c) of the Occupational Safety and Health Act, as an occupational safety and health standard effective October 4, 1974, the amendment to § 1910.93q set out below will supersede these provisions as of January 1, 1975.

Accordingly, upon consideration of the whole record of this proceding, Part 1910 of Title 29, Code of Federal Regulations is amended, effective January 1, 1975, by revision of § 1910.93q to read as follows:

**§ 1910.93q Vinyl chloride.**

(a) *Scope and application.* (1) This section includes requirements for the control of employee exposure to vinyl chloride (chloroethene), Chemical Abstracts Service Registry No. 75015.

(2) This section applies to the manufacture, reaction, packaging, repackaging, storage, handling or use of vinyl chloride or polyvinyl chloride, but does not apply to the handling or use of fabricated products made of polyvinyl chloride.

(3) This section applies to the transportation of vinyl chloride or polyvinyl chloride except to the extent that the Department of Transportation may regulate the hazards covered by this section.

(b) *Definitions.* (1) "Action level" means a concentration of vinyl chloride of 0.5 ppm averaged over an 8-hour work day.

(2) "Assistant Secretary" means the Assistant Secretary of Labor for Occupational Safety and Health, U.S. Department of Labor, or his designee.

(3) "Authorized person" means any person specifically authorized by the employer whose duties require him to enter a regulated area or any person entering such an area as a designated representative of employees for the purpose of exercising an opportunity to observe monitoring and measuring procedures.

(4) "Director" means the Director, National Institute for Occupational Safety and Health, U.S. Department of Health, Education, and Welfare, or his designee.

(5) "Emergency" means any occurrence such as, but not limited to, equipment failure, or operation of a relief device which is likely to, or does, result in massive release of vinyl chloride.

(6) "Fabricated product" means a product made wholly or partly from polyvinyl chloride, and which does not require further processing at temperatures, and for times, sufficient to cause mass melting of the polyvinyl chloride resulting in the release of vinyl chloride.

(7) "Hazardous operation" means any operation, procedure, or activity where a release of either vinyl chloride liquid or gas might be expected as a consequence of the operation or because of an accident in the operation, which would result in an employee exposure in excess of the permissible exposure limit.

(8) "OSHA Area Director" means the Director for the Occupational Safety and Health Administration Area Office having jurisdiction over the geographic area in which the employer's establishment is located.

(9) "Polyvinyl chloride" means polyvinyl chloride homopolymer or copolymer before such is converted to a fabricated product.

(10) "Vinyl chloride" means vinyl chloride monomer.

(c) *Permissible exposure limit.* (1) No employee may be exposed to vinyl chloride at concentrations greater than 1 ppm averaged over any 8-hour period, and

(2) No employee may be exposed to vinyl chloride at concentrations greater than 5 ppm averaged over any period not exceeding 15 minutes.

(3) No employee may be exposed to vinyl chloride by direct contact with liquid vinyl chloride.

(d) *Monitoring.* (1) A program of initial monitoring and measurement shall be undertaken in each establishment to determine if there is any employee exposed, without regard to the use of respirators, in excess of the action level.

(2) Where a determination conducted under paragraph (d)(1) of this section shows any employee exposures, without regard to the use of respirators, in excess of the action level, a program for determining exposures for each such employee shall be established. Such a program:

(i) Shall be repeated at least monthly where any employee is exposed, without regard to the use of respirators, in excess of the permissible exposure limit.

(ii) Shall be repeated not less than quarterly where any employee is exposed, without regard to the use of respirators, in excess of the action level.

(iii) May be discontinued for any employee only when at least two consecutive monitoring determinations, made not less than 5 working days apart, show exposures for that employee at or below the action level.

(3) Whenever there has been a production, process or control change which may result in an increase in the release of vinyl chloride, or the employer has any other reason to suspect that any employee may be exposed in excess of the action level, a determination of employee exposure under paragraph (d)(1) of this section shall be performed.

(4) The method of monitoring and measurement shall have an accuracy (with a confidence level of 95 percent) of not less than plus or minus 50 percent from 0.25 through 0.5 ppm, plus or minus 35 percent from over 0.5 ppm through 1.0 ppm, and plus or minus 25 percent over 1.0 ppm. (Methods meeting these accuracy requirements are available in the "NIOSH Manual of Analytical Methods").

(5) Employees or their designated representatives shall be afforded reasonable opportunity to observe the monitoring and measuring required by this paragraph.

(e) *Regulated area.* (1) A regulated area shall be established where:

(i) Vinyl chloride or polyvinyl chloride is manufactured, reacted, repackaged, stored, handled or used,

(ii) Vinyl chloride concentrations are in excess of the permissible exposure limit.

(2) Access to regulated areas shall be limited to authorized persons. A daily roster shall be made of authorized persons who enter.

(f) *Methods of compliance.* Employee exposures to vinyl chloride shall be controlled to at or below the permissible exposure limit provided in paragraph (c) of this section by engineering, work practice, and personal protective controls as follows:

(1) Feasible engineering and work practice controls shall immediately be used to reduce exposures to at or below the permissible exposure limit.

(2) Wherever feasible engineering and work practice controls which can be instituted immediately are not sufficient to reduce exposures to at or below the permissible exposure limit, they shall nonetheless be used to reduce exposures to the lowest practicable level, and shall be supplemented by respiratory protection in accordance with paragraph (g) of this section. A program shall be established and implemented to reduce exposures to at or below the permissible exposure limit, or to the greatest extent feasible, solely by means of engineering and work practice controls, as soon as feasible.

(3) Written plans for such a program shall be developed and furnished upon request for examination and copying to authorized representatives of the Assistant Secretary and the Director. Such plans shall be updated at least every six months.

(g) *Respiratory protection.* Where respiratory protection is required under this section:

(1) The employer shall provide a respirator which meets the requirements of this paragraph and shall assure that the employee uses such respirator, except that until December 31, 1975, wearing of respirators shall be at the discretion of each employee for exposures not in excess of 25 ppm, measured over any 15-minute period. Until December 31, 1975, each employee who chooses not to wear an appropriate respirator shall be informed at least quarterly of the hazards of vinyl chloride and the purpose, proper use, and limitations of respiratory devices.

(2) Respirators shall be selected from among those jointly approved by the Mining Enforcement and Safety Administration, Department of the Interior, and the National Institute for Occupational Safety and Health under the provisions of 30 CFR Part 11.

(3) A respiratory protection program meeting the requirements of § 1910.134 shall be established and maintained.

(4) Selection of respirators for vinyl chloride shall be as follows:

| Atmospheric concentration of vinyl chloride | Required apparatus |
|---|---|
| (i) Unknown, or above 3,600 ppm | Open-circuit, self-contained breathing apparatus, pressure demand type, with full facepiece. |
| (ii) Not over 3,600 ppm | (A) Combination type C supplied air respirator, pressure demand type, with full or half facepiece, and auxiliary self-contained air supply; or<br>(B) Type C, supplied air respirator continuous flow type, with full or half facepiece, and auxiliary self-contained air supply. |
| (iii) Not over 100 ppm | (A) Combination type C supplied air respirator demand type, with full facepiece, and auxiliary self-contained air supply; or<br>(B) Open-circuit self-contained breathing apparatus with full facepiece, in demand mode; or<br>(C) Type C supplied air respirator, demand type, with full facepiece. |
| (iv) Not over 25 ppm | (A) A powered air-purifying respirator with hood, helmet, full or half facepiece, and a canister which provides a service life of at least 4 hours for concenrations of vinyl chloride up to 25 ppm, or<br>(B) Gas mask, front- or back-mounted canister which provides a service life of at least 4 hours for concentrations of vinyl chloride up to 25 ppm. |
| (v) Not over 10 ppm | (A) Combination type C supplied-air respirator, demand type, with half facepiece, and auxiliary self-contained air supply; or<br>(B) Type C supplied-air respirator, demand type, with half facepiece; or<br>(C) Any chemical cartridge respirator with an organic vapor cartridge which provides a service life of at least 1 hour for concentrations of vinyl chloride up to 10 ppm. |

(5) (i) Entry into unkown concentrations or concentrations greater than 36,000 ppm (lower explosive limit) may be made only for purposes of life rescue; and

(ii) Entry into concentrations of less than 36,000 ppm, but greater than 3,600 ppm may be made only for purposes of life rescue, firefighting, or securing equipment so as to prevent a greater hazard from release of vinyl chloride.

(6) Where air-purifying respirators are used:

(i) Air-purifying cannisters or cartridges shall be replaced prior to the expiration of their service life or the end of the shift in which they are first used, whichever occurs first, and

(ii) A continuous monitoring and alarm system shall be provided where concentrations of vinyl chloride could reasonably exceed the allowable concentrations for the devices in use. Such system shall be used to alert employees when vinyl chloride concentrations exceed the allowable concentrations for the devices in use.

(7) Apparatus prescribed for higher concentrations may be used for any lower concentration.

(h) *Hazardous operations.* (1) Employees engaged in hazardous operations, including entry of vessels to clean polyvinyl chloride residue from vessel walls, shall be provided and required to wear and use;

(i) Respiratory protection in accordance with paragraphs (c) and (g) of this section; and

(ii) Protective garments to prevent skin contact with liquid vinyl chloride or with polyvinyl chloride residue from vessel walls. The protective garments shall be selected for the operation and the possible exposure conditions.

(2) Protective garments shall be provided clean and dry for each use.

(i) *Emergency situations.* A written operational plan for emergency situations shall be developed for each facility storing, handling, or otherwise using vinyl chloride as a liquid or compressed gas. Appropriate portions of the plan shall be implemented in the event of an emergency. The plan shall specifically provide that:

(1) Employees engaged in hazardous operations or correcting situations of existing hazardous releases shall be equipped as required in paragraph (h) of this section;

(2) Other employees not so equipped shall evacuate the area and not return until conditions are controlled by the methods required in paragraph (f) of this section and the emergency is abated.

(j) *Training.* Each employee engaged in vinyl chloride or polyvinyl chloride operations shall be provided training in a program relating to the hazards of vinyl chloride and precautions for its safe use.

(1) The program shall include:

(i) The nature of the health hazard from chronic exposure to vinyl chloride including specifically the carcinogenic hazard;

(ii) The specific nature of operations which could result in exposure to vinyl chloride in excess of the permissible limit and necessary protective steps;

(iii) The purpose for, proper use, and limitations of respiratory protective devices;

(iv) The fire hazard and acute toxicity of vinyl chloride, and the necessary protective steps;

(v) The purpose for and a description of the monitoring program;

(vi) The purpose for, and a description of, the medical surveillance program;

(vii) Emergency procedures;

(viii) Specific information to aid the employee in recognition of conditions which may result in the release of vinyl chloride; and

(ix) A review of this standard at the employee's first training and indoctrination program, and annually thereafter.

(2) All materials relating to the program shall be provided upon request to the Assistant Secretary and the Director.

(k) *Medical surveillance.* A program of medical surveillance shall be instituted for each employee exposed, without regard to the use of respirators, to vinyl chloride in excess of the action level. The program shall provide each such employee with an opportunity for examinations and tests in accordance with this paragraph. All medical examinations and procedures shall be performed by or under the supervision of a licensed physician, and shall be provided without cost to the employee.

(1) At the time of initial assignment, or upon institution of medical surveillance;

(i) A general physical examination shall be performed, with specific attention to detecting enlargement of liver, spleen or kidneys, or dysfunction in these organs, and for abnormalities in skin, connective tissues and the pulmonary system (See Appendix A).

(ii) A medical history shall be taken, including the following topics:

(A) Alcohol intake;

(B) Past history of hepatitis;

(C) Work history and past exposure to potential hepatotoxic agents, including drugs and chemicals;

(D) Past history of blood transfusions; and

(E) Past history of hospitalizations.

(iii) A serum specimen shall be obtained and determinations made of:

(A) Total bilirubin;

(B) Alkaline phosphatase;

(C) Serum glutamic oxalacetic transaminase (SGOT);

(D) Serum glutamic pyruvic transaminase (SGPT); and

(E) Gamma glustamyl transpeptidase.

(2) Examinations provided in accordance with this paragraph shall be performed at least:

(i) Every 6 months for each employee who has been employed in vinyl chloride or polyvinyl chloride manufacturing for 10 years or longer; and

(ii) Annually for all other employees.

(3) Each employee exposed to an emergency shall be afforded appropriate medical surveillance.

(4) A statement of each employee's suitability for continued exposure to vinyl chloride including use of protective equipment and respirators, shall be obtained from the examining physician promptly after any examination. A copy of the physician's statement shall be provided each employee.

(5) If any employee's health would be materially impaired by continued exposure, such employee shall be with-

drawn from possible contact with vinyl chloride.

(6) Laboratory analyses for all biological specimens included in medical examinations shall be performed in laboratories licensed under 42 CFR Part 74.

(7) If the examining physician determines that alternative medical examinations to those required by paragraph (k)(1) of this section will provide at least equal assurance of detecting medical conditions pertinent to the exposure to vinyl chloride, the employer may accept such alternative examinations as meeting the requirements of paragraph (k)(1) of this section, if the employer obtains a statement from the examining physician setting forth the alternative examinations and the rationale for substitution. This statement shall be available upon request for examination and copying to authorized representatives of the Assistant Secretary and the Director.

(l) *Signs and labels.* (1) Entrances to regulated areas shall be posted with legible signs bearing the legend:

CANCER-SUSPECT AGENT AREA AUTHORIZED PERSONNEL ONLY

(2) Areas containing hazardous operations or where an emergency currently exists shall be posted with legible signs bearing the legend:

CANCER-SUSPECT AGENT IN THIS AREA PROTECTIVE EQUIPMENT REQUIRED AUTHORIZED PERSONNEL ONLY

(3) Containers of polyvinyl chloride resin waste from reactors or other waste contaminated with vinyl chloride shall be legibly labeled:

Contaminated with
VINYL CHLORIDE CANCER-SUSPECT AGENT

(4) Containers of polyvinyl chloride shall be legibly labeled:

POLYVINYL CHLORIDE (OR TRADE NAME)
Contains
VINYL CHLORIDE
VINYL CHLORIDE IS A CANCER-SUSPECT AGENT

(5) Containers of vinyl chloride shall be legibly labeled either:

(i)

VINYL CHLORIDE
EXTREMELY FLAMMABLE GAS UNDER PRESSURE
CANCER-SUSPECT AGENT

or (ii) In accordance with 49 CFR Part 173, Subpart H, with the additional legends:

CANCER-SUSPECT AGENT

applied near the labor or placard.

(6) No statement shall appear on or near any required sign, label or instruction which contradicts or detracts from the effect of, any required warning, information or instruction.

(m) *Records.* (1) All records maintained in accordance with this section shall include the name and social security number of each employee where relevant.

(2) Records of required monitoring and measuring, medical records, and authorized personnel rosters, shall be made and shall be available upon request for examination and copying to authorized representatives of the Assistant Secretary and the Director.

(i) Monitoring and measuring records shall:

(A) State the date of such monitoring and measuring and the concentrations determined and identify the instruments and methods used;

(B) Include any additional information necessary to determine individual employee exposures where such exposures are determined by means other than individual monitoring of employees; and

(C) Be maintained for not less than 30 years.

(ii) Authorized personnel rosters shall be maintained for not less than 30 years.

(iii) Medical records shall be maintained for the duration of the employment of each employee plus 20 years, or 30 years, whichever is longer.

(3) In the event that the employer ceases to do business and there is no successor to receive and retain his records for the prescribed period, these records shall be transmitted by registered mail to the Director, and each employee individually notified in writing of this transfer.

(4) Employees or their designated representatives shall be provided access to examine and copy records of required monitoring and measuring.

(5) Former employees shall be provided access to examine and copy required monitoring and measuring records reflecting their own exposures.

(6) Upon written request of any employee, a copy of the medical record of that employee shall be furnished to any physician designated by the employee.

(n) *Reports.* (1) Not later than 1 month after the establishment of a regulated area, the following information shall be reported to the OSHA Area Director. Any changes to such information shall be reported within 15 days.

(i) The address and location of each establishment which has one or more regulated areas; and

(ii) The number of employees in each regulated area during normal operations, including maintenance.

(2) Emergencies, and the facts obtainable at that time, shall be reported within 24 hours to the OSHA Area Director. Upon request of the Area Director, the employer shall submit additional information in writing relevant to the nature and extent of employee exposures and measures taken to prevent future emergencies of similar nature.

(3) Within 10 working days following any monitoring and measuring which discloses that any employee has been exposed, without regard to the use of respirators in excess of the permissible exposure limit, each such employee shall be notified in writing of the results of the exposure measurement and the steps being taken to reduce the exposure to within the permissible exposure limit.

(o) *Effective dates.* (1) Until January 1, 1975, the provisions currently set forth in § 1910.93q of this Part shall apply.

(2) Effective January 1, 1975, the provisions set forth in § 1910.93q of this Part shall apply.

APPENDIX A—SUPPLEMENTARY MEDICAL INFORMATION

When required tests under paragraph (k)(1) of this section show abnormalities, the tests should be repeated as soon as practicable, preferably within 3 to 4 weeks. If tests remain abnormal, consideration should be given to withdrawal of the employee from contact with vinyl chloride, while a more comprehensive examination is made.

Additional tests which may be useful:

A. For kidney dysfunction: urine examination for albumin, red blood cells, and exfoliative abnormal cells.

B. Pulmonary system: Forced vital capacity. Forced expiratory volume at 1 second, and chest roentgenogram (posterior-anterior, 14 x 17 inches).

C. Additional serum tests: Lactic acid dehydrogenase, lactic acid dehydrogenase isoenzyme, protein determination, and protein electrophoresis.

D. For a more comprehensive examination on repeated abnormal serum tests: Hepatitis B antigen, and liver scanning.

(Secs. 6 and 8, 84 Stat. 1596, 1599 (29 U.S.C. 655, 657); Secretary of Labor's Order No. 12-71, 36 FR 8754)

Signed at Washington, D.C., this 1st day of October, 1974.

JOHN STENDER,
*Assistant Secretary of Labor.*

[FR Doc.74-23170 Filed 10-1-74;3:54 pm]

(vi) *Strength of step supports.* When subjected to a load of 400 pounds applied at the approximate center of the step, step frames, or supports and their guides shall be of adequate strength to:

(*a*) Prevent the disengagement of any step roller.

(*b*) Prevent any appreciable misalinement.

(*c*) Prevent any visible deformation of the steps or its support.

(vii) *Prohibition of steps without handholds.* No steps shall be provided unless there is a corresponding handhold above or below it meeting the requirements of subparagraph (4) of this paragraph. If a step is removed for repairs or permanently, the handholds immediately above and below it shall be removed before the lift is again placed in service.

(4) *Handholds*—(i) *Location.* Handholds attached to the belt shall be provided and installed so that they are not less than 4 feet nor more than 4 feet 8 inches above the step tread. These shall be so located as to be available on the both "up" and "down" run of the belt.

(ii) *Size.* The grab surface of the handhold shall be not less than 4½ inches in width, not less than 3 inches in depth, and shall provide 2 inches of clearance from the belt. Fastenings for handholds shall be located not less than 1 inch from the edge of the belt.

(iii) *Strength.* The handhold shall be capable of withstanding, without damage, a load of 300 pounds applied parallel to the run of the belt.

(iv) *Prohibition of handhold without steps.* No handhold shall be provided without a corresponding step. If a handhold is removed permanently or temporarily, the corresponding step and handhold for the opposite direction of travel shall also be removed before the lift is again placed in service.

(v) *Type.* All handholds shall be of the closed type.

(5) *Up limit stops*—(i) *Requirements.* Two separate automatic stop devices shall be provided to cut off the power and apply the brake when a loaded step passes the upper terminal landing. One of these shall consist of a split-rail switch mechanically operated by the step roller and located not more than 6 inches above the top terminal landing. The second automatic stop device may consist of any of the following:

(*a*) Any split-rail switch placed 6 inches above and on the side opposite the first limit switch.

(*b*) An electronic device.

(*c*) A switch actuated by a lever, rod, or plate, the latter to be placed on the "up" side of the head pulley so as to just clear a passing step.

(ii) *Manual reset location.* After the manlift has been stopped by a stop device it shall be necessary to reset the automatic stop manually. The device shall be so located that a person resetting it shall have a clear view of both the "up" and "down" runs of the manlift. It shall not be possible to reset the device from any step or platform.

(iii) *Cut-off point.* The initial limit stop device shall function so that the manlift will be stopped before the loaded step has reached a point 24 inches above the top terminal landing.

(iv) *Electrical requirements.* (*a*) Where such switches open the main motor circuit directly they shall be of the multipole type.

(*b*) Where electronic devices are used they shall be so designed and installed that failure will result in shutting off the power to the driving motor.

(*c*) Where flammable vapors or dusts may be present all electrical installations shall be in accordance with NFPA No. 70–1968 National Electric Code, requirements for such locations.

(*d*) Unless of the oil-immersed type controller contacts carrying the main motor current shall be copper to carbon or equal, except where the circuit is broken at two or more points simultaneously.

(6) *Emergency Stop*—(i) *General.* An emergency stop means shall be provided.

(ii) *Location.* This stop means shall be within easy reach of the ascending and descending runs of the belt.

(iii) *Operation.* This stop means shall be so connected with the control lever or operating mechanism that it will cut off the power and apply the brake when pulled in the direction of travel.

(iv) *Rope.* If rope is used, it shall be not less than three-eighths inch in diameter. Wire rope, unless marlin-covered, shall not be used.

(7) *Instruction and warning signs*—(i) *Instruction signs at landings or belts.* Signs of conspicuous and easily read style giving instructions for the use of the manlift shall be posted at each landing or stenciled on the belt.

(*a*) Such signs shall be of letters not less than 1 inch in height and of a color having high contrast with the surface on which it is stenciled or painted (white or yellow on black or black on white or gray).

(*b*) The instructions shall read approximately as follows:

Face the Belt.
Use the Handholds.
To Stop—Pull Rope.

(ii) *Top floor warning sign and light.* (*a*) At the top floor an illuminated sign shall be displayed bearing the following wording:

"TOP FLOOR—GET OFF"

Signs shall be in block letters not less than 2 inches in height. This sign shall be located within easy view of an ascending passenger and not more than 2 feet above the top terminal landing.

(*b*) In addition to the sign required by subdivision (*a*) of this subdivision, a red warning light of not less than 40-watt rating shall be provided immediately below the upper landing terminal and so located as to shine in the passenger's face.

(iii) *Visitor Warning.* A conspicuous sign having the following legend—AUTHORIZED PERSONNEL ONLY—shall be displayed at each landing. The sign shall be of block letters not less than 2 inches in height and shall be of a color offering high contrast with the background color.

(d) *Operating rules*—(1) *Proper use of manlifts.* No freight, packaged goods, pipe, lumber, or construction material of any kind shall be handled on any manlift.

(e) *Periodic inspection*—(1) *Frequency.* All manlifts shall be inspected by a competent designated person at intervals of not more than 30 days. Limit switches shall be checked weekly. Manlifts found to be unsafe shall not be operated until properly repaired.

(2) *Items covered.* This periodic inspection shall cover but is not limited to the following items:

Steps.
Step Fastenings.
Rails.
Rail Supports and Fastenings.
Rollers and Slides.
Belt and Belt Tension.
Handholders and Fastenings.
Floor Landings.
Guardrails.
Lubrication.
Limit Switches.
Warning Signs and Lights.
Illumination.
Drive Pulley.
Bottom (boot) Pulley and Clearance.
Pulley Supports.
Motor.
Driving Mechanism.
Brake.
Electrical Switches.
Vibration and Misalignment.
"Skip" on up or down run when mounting step (indicating worn gears).

(3) *Inspection log.* A written record shall be kept of findings at each inspection. Records of inspection shall be made available to the Assistant Secretary of Labor or his duly authorized representative.

(SOURCE: ANSI A90.1–1969 Safety Code for Manlifts.)

### § 1910.69 Sources of standards.

| Sec. | Source |
|---|---|
| 1910.66 | ANSI A120.1–1970 Safety Code for Powered Platforms for Exterior Building Maintenance. |
| 1910.67 | ANSI A92.2–1969, American National Standard for Vehicle-Mounted Elevating and Rotating Work Platforms. |
| 1910.68 | ANSI A90.1–1969 Safety Code for Manlifts. |

### § 1910.70 Standards organizations.

Specific standards of the following organizations have been referenced in this subpart. Copies of the standards may be obtained from the issuing organization.

American National Standards Institute, 1430 Broadway, New York, NY 10018.

## Subpart G—Occupational Health and Environmental Control

### § 1910.93 Air contaminants. (Gases, vapors, fumes, dust, and mists.)

(a) Exposures by inhalation, ingestion, skin absorption, or contact to any material or substance (1) at a concentration above those specified in the "Threshold Limit Values of Airborne Contaminants for 1970" of the American Conference of Governmental Industrial Hygienists, listed in Table G–1, except for the American National Standards listed in Table G–2 of this section and

except for values of mineral dusts listed in Table G-3 of this section, and (2) concentrations above those specified in Table G-1, G-2, and G-3 of this section, shall be avoided, or protective equipment shall be provided and used.

(b) To achieve compliance with paragraph (a) of this section, feasible administrative or engineering controls must first be determined and implemented in all cases. In cases where protective equipment, or protective equipment in addition to other measures is used as the method of protecting the employee, such protection must be approved for each specific application by a competent industrial hygienist or other technically qualified source.

TABLE G-I

| Substance | p.p.m.* | mg./M³ ◊ |
|---|---|---|
| Abate | | 15 |
| Acetaldehyde | 200 | 360 |
| Acetic acid | 10 | 25 |
| Acetic anhydride | 5 | 20 |
| Acetone | 1,000 | 2,400 |
| Acetonitrile | 40 | 70 |
| Acetylene dichloride, see 1, 2-Dichloroethylene | | |
| Acetylene tetrabromide | 1 | 14 |
| Acrolein | 0.1 | 0.25 |
| Acrylamide—Skin | | 0.3 |
| Acrylonitrile—Skin | 20 | 45 |
| Aldrin—Skin | | 0.25 |
| Allyl alchol—Skin | 2 | 5 |
| Allyl chloride | 1 | 3 |
| **C Allyl glycidyl ether (AGE) | 10 | 45 |
| Allyl propyl disulfide | 2 | 12 |
| 2-Aminoethanol, see Ethanolamine | | |
| 2-Aminopyridine | 0.5 | 2 |
| **Ammonia | 50 | 35 |
| Ammonium sulfamate (Ammate) | | 15 |
| n-Amyl acetate | 100 | 525 |
| sec-Amyl acetate | 125 | 650 |
| Aniline—Skin | 5 | 19 |
| Anisidine (o, p-isomers)—Skin | | 0.5 |
| Antimony and compounds (as Sb) | | 0.5 |
| ANTU (alpha naphthyl thiourea) | | 0.3 |
| Arsenic and compounds (as As) | | 0.5 |
| Arsine | 0.05 | 0.2 |
| Azinphos-methyl—Skin | | 0.2 |
| Barium (soluble compounds) | | 0.5 |
| p-Benzoquinone, see Quinone | | |
| Benzoyl peroxide | | 5 |
| Benzyl chloride | 1 | 5 |
| Biphenyl, see Diphenyl | | |
| Bisphenol A, see Diglycidyl ether | | |
| Boron oxide | | 15 |
| Boron tribromide | 1 | 10 |
| C Boron trifluoride | 1 | 3 |
| Bromine | 0.1 | 0.7 |
| *Bromine pentafluoride | 0.1 | 0.7 |
| Bromoform—Skin | 0.5 | 5 |
| Butadiene (1, 3-butadiene) | 1,000 | 2,200 |
| Butanethiol, see Butyl mercaptan | | |
| 2-Butanone | 200 | 590 |
| 2-Butoxy ethanol (Butyl Cellosolve)—Skin | 50 | 240 |
| Butyl acetate (n-butyl acetate) | 150 | 710 |
| sec-Butyl acetate | 200 | 950 |
| tert-Butyl acetate | 200 | 950 |
| Butyl alcohol | 100 | 300 |
| sec-Butyl alcohol | 150 | 450 |
| tert-Butyl alcohol | 100 | 300 |
| C Butylamine—Skin | 5 | 15 |
| C tert-Butyl chromate (as $CrO_3$)—Skin | | 0.1 |
| n-Butyl glycidyl ether (BGE) | 50 | 270 |
| *Butyl mercaptan | 0.5 | 1.5 |
| p-tert-Butyltoluene | 10 | 60 |
| Calcium arsenate | | 1 |
| Calcium oxide | | 5 |
| **Camphor (Synthetic) | 2 | |
| Carbaryl (Sevin ®) | | 5 |
| Carbon black | | 3.5 |
| Carbon dioxide | 5,000 | 9,000 |
| Carbon monoxide | 50 | 55 |
| Chlordane—Skin | | 0.5 |
| Chlorinated camphene—Skin | | 0.5 |
| Chlorinated diphenyl oxide | | 0.5 |
| *Chlorine | 1 | 3 |
| Chlorine dioxide | 0.1 | 0.3 |
| C Chlorine trifluoride | 0.1 | 0.4 |

See footnotes at end of table.

TABLE G-I—Con.

| Substance | p.p.m.* | mg./M³ ◊ |
|---|---|---|
| C Chloroacetaldehyde | 1 | 3 |
| α-Chloroacetophenone (phenacylchloride) | 0.05 | 0.3 |
| Chlorobenzene (monochlorobenzene) | 75 | 350 |
| o-Chlorobenzylidene malononitrile (OCBM) | 0.05 | 0.4 |
| Chlorobromomethane | 200 | 1,050 |
| 2-Chloro-1,3-butadiene, see Chloroprene | | |
| Chlorodiphenyl (42 percent Chlorine)—Skin | | 1 |
| Chlorodiphenyl (54 percent Chlorine)—Skin | | 0.5 |
| 1-Chloro-2,3-epoxypropane, see Epichlorhydrin | | |
| 2-Chloroethanol, see Ethylene chlorohydrin | | |
| Chloroethylene, see Vinyl choride | | |
| C Chloroform (trichloromethane) | 50 | 240 |
| 1-Chloro-1-nitropropane | 20 | 100 |
| Chloropicrin | 0.1 | 0.7 |
| Chloroprene (2-chloro-1,3-butadiene)—Skin | 25 | 90 |
| Chromium, sol. chromic, chromous salts as Cr | | 0.5 |
| Metal and insol. salts | | 1 |
| Coal tar pitch volatiles (benzene soluble fraction) anthracene, BaP, phenanthrene, acridine, chrysene, pyrene | | 0.2 |
| Cobalt, metal fume and dust | | 0.1 |
| Copper fume | | 0.1 |
| Dusts and Mists | | 1 |
| Cotton dust (raw) | | 1 |
| Crag® herbicide | | 15 |
| Cresol (all isomers)—Skin | 5 | 22 |
| Crotonaldehyde | 2 | 6 |
| Cumene—Skin | 50 | 245 |
| Cyanide (as CN)—Skin | | 5 |
| *Cyanogen | 100 | |
| Cyclohexane | 300 | 1,050 |
| Cyclohexanol | 50 | 200 |
| Cyclohexanone | 50 | 200 |
| Cyclohexene | 300 | 1,015 |
| Cyclopentadiene | 75 | 200 |
| 2, 4-D | | 10 |
| DDT—Skin | | 1 |
| DDVP, see Dichlorvos | | |
| Decaborane—Skin | 0.05 | 0.3 |
| Demeton® —Skin | | 0.1 |
| Diacetone alcohol (4-hydroxy-4-methyl-2-pentanone) | 50 | 240 |
| 1,2-diaminoethane, see Ethylenediamine | | |
| Diazomethane | 0.2 | 0.4 |
| Diborane | 0.1 | 0.1 |
| Dibutyl phosphate | 1 | 5 |
| Dibutylphthalate | | 5 |
| *C Dichloroacetylene | 0.1 | 0.4 |
| C o-Dichlorobenzene | 50 | 300 |
| p-Dichlorobenzene | 75 | 450 |
| Dichlorodifluoromethane | 1,000 | 4,950 |
| 1,3-Dichloro-5,5-dimethyl hydantoin | | 0.2 |
| 1,1-Dichloroethane | 100 | 400 |
| 1,2-Dichloroethylene | 200 | 790 |
| C Dichloroethyl ether—Skin | 15 | 90 |
| Dichloromethane, see Methylenechloride | | |
| Dichloromonofluoromethane | 1,000 | 4,200 |
| C 1,1-Dichloro-1-nitroethane | 10 | 60 |
| 1,2-Dichloropropane, see Propylenedichloride | | |
| Dichlorotetrafluoroethane | 1,000 | 7,000 |
| Dichlorvos (DDVP)—Skin | | 1 |
| Dieldrin—Skin | | 0.25 |
| Diethylamine | 25 | 75 |
| Diethylamino ethanol—Skin | 10 | 50 |
| **C Diethylene triamine—Skin | 10 | 42 |
| Diethylether, see Ethyl ether | | |
| Difluorodibromomethane | 100 | 860 |
| C Diglycidyl ether (DGE) | 0.5 | 2.8 |
| Dihydroxybenzene, see Hydroquinone | | |
| Diisobutyl ketone | 50 | 290 |
| Diisopropylamine—Skin | 5 | 20 |
| Dimethoxymethane, see Methylal | | |
| Dimethyl acetamide—Skin | 10 | 35 |
| Dimethylamine | 10 | 18 |
| Dimethylaminobenzene, see Xylidene | | |
| Dimethylaniline(N-dimethylaniline)—Skin | 5 | 25 |
| Dimethylbenzene, see Xylene | | |
| Dimethyl 1,2-dibromo-2,2-dichloroethyl phosphate, (Dibrom) | | 3 |
| Dimethylformamide—Skin | 10 | 30 |
| 2,6-Dimethylheptanone, see Diisobutyl ketone | | |
| 1,1-Dimethylhydrazine—Skin | 0.5 | 1 |
| Dimethylphthalate | | 5 |

TABLE G-I—Con.

| Substance | p.p.m.* | mg./M³ ◊ |
|---|---|---|
| Dimethylsulfate—Skin | 1 | 5 |
| Dinitrobenzene (all isomers)—Skin | | 1 |
| Dinitro-o-cresol—Skin | | 0.2 |
| Dinitrotoluene—Skin | | 1.5 |
| Dioxane (Diethylene dioxide)—Skin | 100 | 360 |
| Diphenyl | 0.2 | 1 |
| Diphenyl amine | | 10 |
| Diphenylmethane diisocyanate (see Methylene bisphenyl isocyanate (MDI) | | |
| Dipropylene glycol methyl ether—Skin | 100 | 600 |
| Di-sec, octyl phthalate (Di-2-ethylhexylphthalate) | | 5 |
| *Endosulfan (Thiodan ®)—Skin | | 0.1 |
| Endrin—Skin | | 0.1 |
| Epichlorhydrin—Skin | 5 | 19 |
| EPN—Skin | | 0.5 |
| 1,2-Epoxypropane, see Propyleneoxide | | |
| 2,3-Epoxy-1-propanol, see Glycidol | | |
| Ethanethiol, see Ethylmercaptan | | |
| Ethanolamine | 3 | 6 |
| 2-Ethoxyethanol—Skin | 200 | 740 |
| 2-Ethoxyethylacetate (Cellosolve acetate)—Skin | 100 | 540 |
| Ethyl acetate | 400 | 1,400 |
| Ethyl acrylate—Skin | 25 | 100 |
| Ethyl alcohol (ethanol) | 1,000 | 1,900 |
| Ethylamine | 10 | 18 |
| Ethyl sec-amyl ketone (5-methyl-3-heptanone) | 25 | 130 |
| Ethyl benzene | 100 | 435 |
| Ethyl bromide | 200 | 890 |
| Ethyl butyl ketone (3-Heptanone) | 50 | 230 |
| Ethyl chloride | 1,000 | 2,600 |
| Ethyl ether | 400 | 1,200 |
| Ethyl formate | 100 | 300 |
| Ethyl mercaptan | 0.5 | 1 |
| Ethyl silicate | 100 | 850 |
| Ethylene chlorohydrin—Skin | 5 | 16 |
| Ethylenediamine | 10 | 25 |
| Ethylene dibromide, see 1,2-Dibromoethane | | |
| Ethylene dichloride, see 1,2-Dichloroethane | | |
| C Ethylene glycol dinitrate and/or Nitroglycerin—Skin | ◊ 0.2 | |
| Ethylene glycol monomethyl ether acetate, see Methyl cellosolve acetate | | |
| Ethylene imine—Skin | 0.5 | 1 |
| Ethylene oxide | 50 | 90 |
| Ethylidine chloride, see 1,1-Dichloroethane | | |
| N-Ethylmorpholine—Skin | 20 | 94 |
| Ferbam | | 15 |
| Ferrovanadium dust | | 1 |
| Fluoride (as F) | | 2.5 |
| Fluorine | 0.1 | 0.2 |
| Fluorotrichloromethane | 1,000 | 5,600 |
| Formic acid | 5 | 9 |
| Furfural—Skin | 5 | 20 |
| Furfuryl alcohol | 50 | 200 |
| Glycidol (2,3-Epoxy-1-propanol) | 50 | 150 |
| Glycol monoethyl ether, see 2-Ethoxyethanol | | |
| Guthion, ® see Azinphos-methyl | | |
| Hafnium | | 0.5 |
| Heptachlor—Skin | | 0.5 |
| Heptane (n-heptane) | 500 | 2,000 |
| Hexachloroethane—Skin | 1 | 10 |
| Hexachloronaphthalene—Skin | | 0.2 |
| Hexane (n-hexane) | 500 | 1,800 |
| 2-Hexanone | 100 | 410 |
| Hexone (Methyl isobutyl ketone) | 100 | 410 |
| sec-Hexyl acetate | 50 | 300 |
| Hydrazine—Skin | 1 | 1.3 |
| Hydrogen bromide | 3 | 10 |
| C Hydrogen chloride | 5 | 7 |
| Hydrogen cyanide—Skin | 10 | 11 |
| Hydrogen peroxide | 1 | 1.4 |
| Hydrogen selenide | 0.05 | 0.2 |
| Hydroquinone | | 2 |
| *Indene | 10 | 45 |
| Indium and compounds, as In | | 0.1 |
| C Iodine | 0.1 | 1 |
| Iron oxide fume | | 10 |
| Iron salts, soluble, as Fe | | 1 |
| Isoamyl acetate | 100 | 525 |
| Isoamyl alcohol | 100 | 360 |
| Isobutyl acetate | 150 | 700 |
| Isobutyl alcohol | 100 | 300 |
| Isophorone | 25 | 140 |
| Isopropyl acetate | 250 | 950 |
| Isopropyl alcohol | 400 | 980 |
| Isopropylamine | 5 | 12 |

TABLE G-I—Con.

| Substance | p.p.m.[a] | mg./M³ [b] |
|---|---|---|
| Isopropylether | 500 | 2,100 |
| Isopropyl glycidyl ether (IGE) | 50 | 240 |
| Ketene | 0.5 | 0.9 |
| Lead arsenate | | 0.15 |
| Lindane—Skin | | 0.5 |
| Lithium hydride | | 0.025 |
| L.P.G. (liquified petroleum gas) | 1,000 | 1,800 |
| Magnesium oxide fume | | 15 |
| Malathion—Skin | | 15 |
| Maleic anhydride | 0.25 | 1 |
| C Manganese and compounds, as Mn | | 5 |
| Mesityl oxide | 25 | 100 |
| Methanethiol, see Methyl mercaptan | | |
| Methoxychlor | | 15 |
| 2-Methoxyethanol, see Methyl cellosolve | | |
| Methyl acetate | 200 | 610 |
| Methyl acetylene (propyne) | 1,000 | 1,650 |
| Methyl acetylene-propadiene mixture (MAPP) | 1,000 | 1,800 |
| Methyl acrylate—Skin | 10 | 35 |
| Methylal (dimethoxymethane) | 1,000 | 3,100 |
| Methyl alcohol (methanol) | 200 | 260 |
| Methylamine | 10 | 12 |
| Methyl amyl alcohol, see Methyl isobutyl carbinol | | |
| *Methyl isoamyl ketone | 100 | 475 |
| Methyl (n-amyl) ketone (2-Heptanone) | 100 | *465 |
| C Methyl bromide—Skin | 20 | 80 |
| Methyl butyl ketone, see 2-Hexanone | | |
| Methyl cellosolve—Skin | 25 | 80 |
| Methyl cellosolve acetate—Skin | 25 | 120 |
| Methyl chloroform | 350 | 1,900 |
| Methylcyclohexane | 500 | 2,000 |
| Methylcyclohexanol | 100 | 470 |
| o-Methylcyclohexanone—Skin | 100 | 460 |
| Methyl ethyl ketone (MEK), see 2-Butanone | | |
| Methyl formate | 100 | 250 |
| Methyl Iodide—Skin | 5 | 28 |
| Methyl isobutyl carbinol—Skin | 25 | 100 |
| Methyl isobutyl ketone, see Hexone | | |
| Methyl isocyanate—Skin | 0.02 | 0.05 |
| *Methyl mercaptan | 0.5 | 1 |
| Methyl methacrylate | 100 | 410 |
| Methyl propyl ketone, see 2-Pentanone | | |
| C Methyl silicate | 5 | 30 |
| C α Methyl styrene | 100 | 480 |
| C Methylene bisphenyl isocyanate (MDI) | 0.02 | 0.2 |
| Molybdenum: | | |
| Soluble compounds | | 5 |
| Insoluble compounds | | 15 |
| Monomethyl aniline—Skin | 2 | 9 |
| C Monomethyl hydrazine—Skin | 0.2 | 0.35 |
| Morpholine—Skin | 20 | 70 |
| Naphtha (coaltar) | 100 | 400 |
| Naphthalene | 10 | 50 |
| Nickel carbonyl | 0.001 | 0.007 |
| Nickel, metal and soluble cmpds, as Ni | | 1 |
| Nicotine—Skin | | 0.5 |
| Nitric acid | 2 | 5 |
| Nitric oxide | 25 | 30 |
| p-Nitroaniline—Skin | 1 | 6 |
| Nitrobenzene—Skin | 1 | 5 |
| p-Nitrochlorobenzene—Skin | | 1 |
| Nitroethane | 100 | 310 |
| Nitrogen dioxide | 5 | 9 |
| Nitrogen trifluoride | 10 | 29 |
| Nitroglycerin—Skin | 0.2 | 2 |
| Nitromethane | 100 | 250 |
| 1-Nitropropane | 25 | 90 |
| 2-Nitropropane | 25 | 90 |
| Nitrotoluene—Skin | 5 | 30 |
| Nitrotrichloromethane, see Chloropicrin | | |
| Octachloronaphthalene—Skin | | 0.1 |
| *Octane | 400 | 1,900 |
| *Oil mist, particulate | | *5 |
| Osmium tetroxide | | 0.002 |
| Oxalic acid | | 1 |
| Oxygen difluoride | 0.05 | 0.1 |
| Ozone | 0.1 | 0.2 |
| Paraquat—Skin | | 0.5 |
| Silver, metal and soluble compounds | | 0.01 |
| Sodium fluoroacetate (1080)—Skin | | 0.05 |
| Sodium hydroxide | | 2 |
| Stibine | 0.1 | 0.5 |
| *Stoddard solvent | 200 | 1,150 |
| Strychnine | | 0.15 |
| Sulfur dioxide | 5 | 13 |
| Sulfur hexafluoride | 1,000 | 6,000 |

TABLE G-I—Con.

| Substance | p.p.m.[a] | mg./M³ [b] |
|---|---|---|
| Sulfuric acid | | 1 |
| Sulfur monochloride | 1 | 6 |
| Sulfur pentafluoride | 0.025 | 0.25 |
| Sulfuryl fluoride | 5 | 20 |
| Systox, see Demeton ® | | |
| 2,4,5T | | 10 |
| Tantalum | | 5 |
| TEDP—Skin | | 0.2 |
| Tellurium | | 0.1 |
| Tellurium hexafluoride | 0.02 | 0.2 |
| TEPP—Skin | | 0.05 |
| C Terphenyls | 1 | 9 |
| 1,1,1,2-Tetrachloro-2,2-difluoroethane | 500 | 4,170 |
| 1,1,2,2-Tetrachloro-1,2-difluoroethane | 500 | 4,170 |
| 1,1,2,2-Tetrachloroethane—Skin | 5 | 35 |
| Tetrachloroethylene, see Perchloroethylene | | |
| Tetrachloromethane, see Carbon tetrachloride | | |
| Tetrachloronaphthalene—Skin | | 2 |
| Tetraethyl lead (as Pb)—Skin | | /0.100 |
| Tetrahydrofuran | 200 | 590 |
| Tetramethyl lead (as Pb)—Skin | | /0.150 |
| Tetramethyl succinonitrile—Skin | 0.5 | 3 |
| Tetranitromethane | 1 | 8 |
| Tetryl (2,4,6-trinitrophenylmethylnitramine)—Skin | | 1.5 |
| Thallium (soluble compounds)—Skin as Tl | | 0.1 |
| Thiram | | 5 |
| Tin (inorganic cmpds, except $SnH_4$ and $SnO_2$) | | 2 |
| Tin (organic cmpds) | | 0.1 |
| C Toluene-2,4-diisocyanate | 0.02 | 0.14 |
| o-Toluidine—Skin | 5 | 22 |
| Toxaphene, see Chlorinated camphene | | |
| Tributyl phosphate | | 5 |
| 1,1,1-Trichloroethane see Methyl chloroform | | |
| 1,1,2-Trichloroethane—Skin | 10 | 45 |
| Parathion—Skin | | 0.1 |
| Pentaborane | 0.005 | 0.01 |
| Pentachloronaphthalene—Skin | | 0.5 |
| Pentachlorophenol—Skin | | 0.5 |
| *Pentane | 500 | 1,500 |
| 2-Pentanone | 200 | 700 |
| Perchloromethyl mercaptan | 0.1 | 0.8 |
| Perchloryl fluoride | 3 | 13.5 |
| Phenol—Skin | 5 | 19 |
| p-Phenylene diamine—Skin | | 0.1 |
| Phenyl ether (vapor) | 1 | 7 |
| Phenyl ether-biphenyl mixture (vapor) | 1 | 7 |
| Phenylethylene, see Styrene | | |
| Phenyl glycidyl ether (PGE) | 10 | 60 |
| Phenylhydrazine—Skin | 5 | 22 |
| Phosdrin (Mevinphos ®)—Skin | | 0.1 |
| Phosgene (carbonyl chloride) | 0.1 | 0.4 |
| Phosphine | 0.3 | 0.4 |
| Phosphoric acid | | 1 |
| Phosphorus (yellow) | | 0.1 |
| Phosphorus pentachloride | | 1 |
| Phosphorus pentasulfide | | 1 |
| Phosphorus trichloride | 0.5 | 3 |
| Pthalic anhydride | 2 | 12 |
| Picric acid—Skin | | 0.1 |
| Pival ® (2-Pivalyl-1,3-indandione) | | 0.1 |
| Platinum (Soluble Salts) as Pt | | 0.002 |
| Propargyl alcohol—Skin | 1 | |
| n-Propyl acetate | 200 | 840 |
| Propyl alcohol | 200 | 500 |
| n-Propyl nitrate | 25 | 110 |
| Propylene dichloride | 75 | 350 |
| Propylene imine—Skin | 2 | 5 |
| Propylene oxide | 100 | 240 |
| Propyne, see Methylacetylene | | |
| Pyrethrum | | 5 |
| Pyridine | 5 | 15 |
| Quinone | 0.1 | 0.4 |
| RDX—Skin | | 1.5 |
| Rhodium, Metal fume and dusts, as Rh | | 0.1 |
| Soluble salts | | 0.001 |
| Ronnel | | 10 |
| Rotenone (commercial) | | 5 |
| Selenium compounds (as Se) | | 0.2 |
| Selenium hexafluoride | 0.05 | 0.4 |
| Trichloromethane, see Chloroform | | |
| Trichloronaphthalene—Skin | | 5 |
| 1,2,3-Trichloropropane | 50 | 300 |
| 1,1,2-Trichloro 1,2,2-trifluoroethane | 1,000 | 7,600 |
| Triethylamine | 25 | 100 |
| Trifluoromonobromomethane | 1,000 | 6,100 |

TABLE G-I—Con.

| Substance | p.p.m.[a] | mg./M³ [b] |
|---|---|---|
| *Trimethyl benzene | 25 | 120 |
| 2,4,6-Trinitrophenol, see Picric acid | | |
| 2,4,6-Trinitrophenylmethylnitramine, see Tetryl | | |
| Trinitrotoluene—Skin | | 1.5 |
| Triorthocresyl phosphate | | 0.1 |
| Triphenyl phosphate | | 3 |
| Tungsten and compounds, as W: | | |
| Soluble | | 1 |
| Insoluble | | 5 |
| Turpentine | 100 | 560 |
| Uranium (natural) sol. and insol. compounds as U | | 0.2 |
| C Vanadium: | | |
| $V_2O_5$ dust | | 0.5 |
| $V_2O_5$ fume | | 0.1 |
| Vinyl benzene, see Styrene | | |
| **C Vinyl chloride | 500 | 1,300 |
| Vinylcyanide, see Acrylonitrile | | |
| Vinyl toluene | 100 | 480 |
| Warfarin | | 0.1 |
| Xylene (xylol) | 100 | 435 |
| Xylidine—Skin | 5 | 25 |
| Yttrium | | 1 |
| Zinc chloride fume | | 1 |
| Zinc oxide fume | | 5 |
| Zirconium compounds (as Zr) | | 5 |

*1970 Addition.

[a] Parts of vapor or gas per million parts of contaminated air by volume at 25° C. and 760 mm. Hg pressure.

[b] Approximate milligrams of particulate per cubic meter of air.

(No footnote "c" is used to avoid confusion with ceiling value notations.)

[d] An atmospheric concentration of not more than 0.02 p.p.m., or personal protection may be necessary to avoid headache.

[e] As sampled method that does not collect vapor.

[f] For control of general room air, biologic monitoring is essential for personnel control.

TABLE G-2

| | 8-hour time weighted average |
|---|---|
| Benzene (Z37.4–1969) | 10 p.p.m. |
| Beryllium and beryllium compounds (Z37.29–1970) | 0.002 mg./M³. |
| Cadmium dust (as Cd) (Z37.5–1970) | 0.2 mg./M³. |
| Cadmium fume (as Cd) (Z37.5–1970) | 0.1 mg./M³. |
| Carbon disulfide (Z37.3–1968) | 20 p.p.m. |
| Carbon tetrachloride (Z37.17–1967) | 10 p.p.m. |
| Ethylene dibromide (Z37.31–1970) | 20 p.p.m. |
| Ethylene dichloride (Z37.21–1969) | 50 p.p.m. |
| Formaldehyde (Z37.16–1967) | 3 p.p.m. |
| Hydrogen fluoride (Z37.28–1969) | 3 p.p.m. |
| Fluoride as dust (Z37.28–1966) | 2.5 mg./M³. |
| Lead and its inorganic compounds (Z37.11–1969) | 0.2 mg./M³. |
| Methyl chloride (Z37.18–1969) | 100 p.p.m. |
| Methylene chloride (Z37.23–1969) | 500 p.p.m. |
| Organo (alkyl) mercury (Z37.30–1969) | 0.01 mg./M³. |
| Styrene (Z37.12–1969) | 100 p.p.m. |
| Tetrachloroethylene (Z37.22–1967) | 100 p.p.m. |
| Toluene (Z37.12–1967) | 200 p.p.m. |

| | Acceptable ceiling concentration |
|---|---|
| Hydrogen sulfide (Z37.2–1966) | 20 p.p.m. |
| Chromic acid and chromates (Z37.3–1971) | 1 mg./10M³. |
| Mercury (Z37.8–1971) | 1 mg./10M³. |

See footnotes at end of table.

TABLE G-3—MINERAL DUSTS

| Substance | Mppcf [a] | Mg/M [3] |
|---|---|---|
| Silica: | | |
| Crystalline: | | |
| Quartz (respirable) | 250 [f] | 10mg/M [3] ÷ |
| | %SiO₂+5 | %SiO₂+2 |
| Quartz (total dust) | | 30mg/M [3] |
| | | %SiO₂+2 |
| Cristobalite: Use ½ the value calculated from the count or mass formulae for quartz. | | |
| Tridymite: Use ½ the value calculated from the formulae for quartz. | | |
| Amorphous, including natural diatomaceous earth | 20 | 80mg/M [3] |
| | | %SiO₂ |
| Tremolite | 5 | 20mg/M [3] |
| | | %SiO₂ |
| Silicates (less than 1% crystalline silica): | | |
| Asbestos—12 fibers per milliliter greater than 5 microns in length [g] or | 2 | |
| Mica | 20 | |
| Soapstone | 20 | |
| Talc | 20 | |
| Portland cement | 50 | |
| Graphite (natural) | 15 | |
| Coal dust (respirable fraction less than 5% SiO₂) | | 2.4mg/M [3] or |
| For more than 5% SiO₂ | | 10mg/M [3] ÷ |
| | | %SiO₂+2 |
| Inert or Nuisance Dust: | | |
| Respirable fraction | 15 | 5mg/M [3] |
| Total dust | 50 | 15mg/M [3] |

NOTE: Conversion factors—
mppcf×35.3=million particles per cubic meter
=particles per c.c.

[a] Millions of particles per cubic foot of air, based on impinger samples counted by light-field technics.

[f] The percentage of crystalline silica in the formula is the amount determined from air-borne samples, except in those instances in which other methods have been shown to be applicable.

[g] As determined by the membrane filter method at 430 × phase contrast magnification.

[h] Both concentration and percent quartz for the application of this limit are to be determined from the fraction passing a size-selector with the following characteristics:

| Aerodynamic diameter (unit density sphere) | Percent passing selector |
|---|---|
| 2 | 90 |
| 2.5 | 75 |
| 3.5 | 50 |
| 5.0 | 25 |
| 10 | 0 |

The measurements under this note refer to the use of an AEC instrument. If the respirable fraction of coal dust is determined with a MRE the figure corresponding to that of 2.4 Mg/M [3] in the table for coal dust is 4.5 Mg/M [3]

### § 1910.94 Ventilation.

(a) *Abrasive blasting*—(1) *Definitions applicable to this paragraph.*—(i) *Abrasive.* A solid substance used in an abrasive blasting operation.

(ii) *Abrasive-blasting respirator.* A continuous flow air-line respirator constructed so that it will cover the wearer's head, neck, and shoulders to protect him from rebounding abrasive.

(iii) *Blast cleaning barrel.* A complete enclosure which rotates on an axis, or which has an internal moving tread to tumble the parts, in order to expose various surfaces of the parts of the action of an automatic blast spray.

(iv) *Blast cleaning room.* A complete enclosure in which blasting operations are performed and where the operator works inside of the room to operate the blasting nozzle and direct the flow of the abrasive material.

(v) *Blasting cabinet.* An enclosure where the operator stands outside and operates the blasting nozzle through an opening or openings in the enclosure.

(vi) *Clean air.* Air of such purity that it will not cause harm or discomfort to an individual if it is inhaled for extended periods of time.

(vii) *Dust collector.* A device or combination of devices for separating dust from the air handled by an exhaust ventilation system.

(viii) *Exhaust ventilation system.* A system for removing contaminated air from a space, comprising two or more of the following elements (*a*) enclosure or hood, (*b*) duct work, (*c*) dust collecting equipment, (*d*) exhauster, and (*e*) discharge stack.

(ix) *Particulate-filter respirator.* An air purifying respirator, commonly referred to as a dust or a fume respirator, which removes most of the dust or fume from the air passing through the device.

(x) *Respirable dust.* Airborne dust in sizes capable of passing through the upper respiratory system to reach the lower lung passages.

(xi) *Rotary blast cleaning table.* An enclosure where the pieces to be cleaned are positioned on a rotating table and are passed automatically through a series of blast sprays.

(xii) *Abrasive blasting.* The forcible application of an abrasive to a surface by pneumatic pressure, hydraulic pressure, or centrifugal force.

(2) *Dust hazards from abrasive blasting.* (i) Abrasives and the surface coatings on the materials blasted are shattered and pulverized during blasting operations and the dust formed will contain particles of respirable size. The composition and toxicity of the dust from these sources shall be considered in making an evaluation of the potential health hazards.

(ii) The concentration of respirable dust or fume in the breathing zone of the abrasive-blasting operator or any other worker shall be kept below the levels specified in § 1910.93.

(iii) Organic abrasives which are combustible shall be used only in automatic systems. Where flammable or explosive dust mixtures may be present, the construction of the equipment, including the exhaust system and all electric wiring shall conform to the requirements of American National Standard Installation of Blower and Exhaust Systems for Dust, Stock, and Vapor Removal or Conveying, Z33.1–1961 (NFPA 91–1961), and American National Standard National Electrical Code, C1–1968 (NFPA 70–1968). The blast nozzle shall be bonded and grounded to prevent the buildup of static charges. Where flammable or explosive dust mixtures may be present, the abrasive blasting enclosure, the ducts, and the dust collector shall be constructed with loose panels or explosion venting areas, located on sides away from any occupied area, to provide for pressure relief in case of explosion, following the principles set forth in the National Fire Protection Association Explosion Venting Guide, NFPA 68–1954.

(3) *Blast-cleaning enclosures.* (i) Blast-cleaning enclosures shall be exhaust ventilated in such a way that a continuous inward flow of air will be maintained at all openings in the enclosure, during the blasting operation.

(*a*) All air inlets and access openings shall be baffled or so arranged that by the combination of inward air flow and baffling the escape of abrasive or dust particules into an adjacent work area will be minimized and visible spurts of dust will not be observed.

(*b*) The rate of exhaust shall be sufficient to provide prompt clearance of the dust-laden air within the enclosure after the cessation of blasting.

(*c*) Before the enclosure is opened, the blast shall be turned off and the exhaust system shall be run for a sufficient period of time to remove the dusty air within the enclosure.

(*d*) Safety glass protected by screening shall be used in observation windows, where hard deep-cutting abrasives are used.

(*e*) Slit abrasive-resistant baffles shall be installed in multiple sets at all small access openings where dust might escape, and shall be inspected regularly and replaced when needed.

(*f*) Doors shall be flanged and tight when closed.

(2) Doors on blast-cleaning rooms shall be operable from both inside and outside, except that where there is a small operator access door, the large work access door may be closed or opened from the outside only.

(4) *Exhaust ventilation systems.* (i) The construction, installation, inspection, and maintenance of exhaust systems shall conform to the principles and requirements set forth in American National Standard Fundamentals Governing the Design and Operation of Local Exhaust Systems, Z9.2–1960, and ANSI Z33.1–1961.

(*a*) When dust leaks are noted, repairs shall be made as soon as possible.

(*b*) The static pressure drop at the exhaust ducts leading from the equipment shall be checked when the installation is completed and periodically thereafter to assure continued satisfactory operation. Whenever an appreciable change in the pressure drop indicates a partial blockage, the system shall be cleaned and returned to normal operating condition.

(ii) In installations where the abrasive is recirculated, the exhaust ventilation system for the blasting enclosure shall not be relied upon for the removal of fines from the spent abrasive instead of an abrasive separator. An abrasive separator shall be provided for the purpose.

(iii) The air exhausted from blast-cleaning equipment shall be discharged through dust collecting equipment. Dust collectors shall be set up so that the accumulated dust can be emptied and removed without contaminating other working areas.

(5) *Personal protective equipment.* (i) Only respiratory protective equipment

## Title 29—Labor

## CHAPTER XVII—OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION, DEPARTMENT OF LABOR

## PART 1910—OCCUPATIONAL SAFETY AND HEALTH STANDARDS

### Carcinogens

Pursuant to section 6(b) and (c) of the Williams-Steiger Occupational Safety and Health Act of 1970 (29 U.S.C. 655) and Secretary of Labor's Order No. 12–71 (36 FR 8754), Part 1910 of Title 29, Code of Federal Regulations, is hereby amended in the manner set forth below, in order to provide standards dealing with the exposure of employees to certain substances that are known to cause cancer.

*Background.* On May 22, 1972, the Deputy Assistant Secretary of Labor for Occupational Safety and Health requested information from the Director of the National Institute for Occupational Safety and Health (NIOSH) on nine substances alleged to be carcinogens. As part of his effort to gain the best available scientific data, the Director published on July 6, 1972, at 37 FR 13285, a request for information concerning 15 substances. The data, arguments, and conclusions received by NIOSH were made available to the Occupational Safety and Health Administration.

On January 4, 1973, a petition for an emergency temporary standard from the Oil, Chemical, and Atomic Workers Union (OCAW) and Health Research Group (HRG) was received by the Department of Labor. The petition contained relevant information on the danger of exposure to 10 carcinogens, and suggested regulations to prevent worker exposure to the substances.

On February 9, 1973, a notice was published in the FEDERAL REGISTER (38 FR 4037) of the receipt of the petition for issuance of an emergency temporary standard, and information was requested from interested persons on the issues involved. In response to the notice, more than 50 written comments were received.

An emergency temporary standard on carcinogens was promulgated on May 3, 1973, at 38 FR 10929. The standard concerned work practices and controls designed to protect employees from exposure to 14 carcinogenic substances.

A standard advisory committee on carcinogens was appointed and began its meetings on June 25, 1973. The members of the committee represented employers, employees, Federal and state agencies and professionals. The committee terminated its meetings on August 24, 1973, and submitted to the Assistant Secretary of Labor for Occupational Safety and Health its recommendations for a standard on certain carcinogens on August 27, 1973. The recommendations were published in the FEDERAL REGISTER on September 7, 1973 (38 FR 24375).

This rulemaking proceeding was commenced under section 6 (b) and (c) of the Act, with the emergency temporary standard serving as a proposal as required by section 6(c)(3) of the Act. Notice of the proceeding was published in the FEDERAL REGISTER on July 16, 1973 (38 FR 18900). On July 27, 1973, a revision of the emergency temporary standard was published at 38 FR 20074, and an amended notice of rulemaking proceeding was published at 38 FR 22141, on August 16, 1973.

The notices invited interested persons to submit, prior to September 5, written comments, data and arguments concerning the proposals, and also provided for the presentation of oral testimony at a public hearing scheduled for September 11–14, 1973. Numerous written comments were received and about 36 parties testified at the hearing. The record of the hearing was initially held open until September 28, for additional comments. After the close and certification of the record by the administrative law judge, additional comments mailed on or before September 28 were received. On October 2 the judge reopened the record for the limited purpose of including these additional comments. On October 15, the judge closed the proceeding and forwarded the certified record to the Assistant Secretary of Labor for Occupational Safety and Health for final decision.

A final environmental impact statement on the proposed standard on carcinogens was filed with the Council on Environmental Quality on October 2, 1973, and copies were distributed to appropriate agencies. In a letter dated November 2, 1973, the Council pointed out alleged deficiencies in the statement filed. Pursuant to that letter, a supplement to the statement was sent to the Council on November 29, 1973, with a request for a waiver of the full, 30-day review period. By letter dated December 10, 1973, the Council advised that the request had been denied. Notice of the filing of the supplement was published by the Council on December 14, 1973 (38 FR 34488).

The following are the major issues raised in the record of this proceeding:

(1) *Selection of carcinogens.* Some participants in this proceeding have demanded to know the criteria for the selection of the 14 substances for regulation. As the written submission of Uniroyal Chemical notes, thirteen compounds derive from Appendix A to the 1972 TLV pamphlet published by the American Conference of Government Industrial Hygienists (ACGIH). Alpha-Naphthylamine, which is not in the appendix, has been added because it has frequently been found, in industrial experience and in epidemiologic studies, together with beta-naphthylamine, and because experimental animal studies demonstrate its independent carcinogencity. Dimethyl sulfate, which is in the appendix, is not included in the standards because it was concluded after consideration of the relevant literature that the documentation of its carcinogenicity was inadequate. The substances listed by ACGIH (except one) were selected in order to take advantage of the work and judgment of that group. Also, ten of the fourteen substances were proposed to the Occupational Safety and Health Administration (OSHA) for regulation by OCAW and HRG in their petition.

(2) *Documentation of carcinogenicity.* The National Institute for Occupational Safety and Health (NIOSH), as official scientific advisor to OSHA, submitted to OSHA fourteen hazard review documents; one for each of the substances included in the standards. Each hazard review document contains a summary and evaluation of information and data obtained by NIOSH, including experimental animal and epidemiologic data. All but one of the substances are considered by ACGIH to be carcinogenic in man and/or animals.

In promulgating these standards, OSHA has relied extensively but not exclusively, on the hazard review documents prepared by NIOSH. Some of the substances are recognized as human carcinogens by some employers participating in this proceeding. For instance, although Young Aniline Works apparently takes issue with the studies which demonstrated Benzidine to be a human carcinogen, the Benzidine Task Force of the Synthetic Organic Chemical Manufacturers Association does not oppose OSHA considering benzidine as carcinogenic to humans.

The essence of the NIOSH hazard review documents follows.

*2-Acetylaminofluorene.* Experimental animal investigations involving rats, mice, rabbits, dogs, hamsters and fowl have demonstrated the carcinogenicity of 2-Acetylaminofluorene (2-AAF). Investigations into the mechanism whereby 2-Acetylaminofluorene exerts its carcinogenic effect have demonstrated that the N-hydroxylated metabolite, N-hydroxy-2-AAF, was produced in several animal species and was more carcinogenic than the parent compound. The National Cancer Institute (NCI) demonstrated that humans also metabolize this substance to the same carcinogenic metabolite. From these findings, it seems reasonable to conclude that 2-AAF, which has been shown to be carcinogenic in many animal species, is carcinogenic in man.

*4-Aminodiphenyl.* The potential of 4-Aminodiphenyl (4-ADP) to induce bladder cancer in humans has been established in epidemiologic studies conducted by Melick et al. and Koss et al. Deichmann & Radomski considered 4-ADP to possess a relative carcinogenic potential for the dog 6 times greater than that of beta-Naphthylamine, 17 times greater than that of 4-Nitrobiphenyl and 27 times greater than that of Benzidine. In addition, the carcinogenicity of 4-ADP has been well-established in the open scientific literature with demonstrated potential for malignant tumor induction in rabbits and mice. The accumulated experimental and epidemiologic evidence have demonstrated 4-Aminodiphenyl may be the most hazardous aromatic amine regarding carcinogenic potential.

*Benzidine.* Benzidine was demonstrated to be carcinogenic in experimental animal investigations involving

s, dogs, hamsters, and mice. Epidemiic investigations of worker populans exposed to Benzidine have clearly nonstrated that this substance and salts are also carcinogenic in humans. e incidence of urinary bladder can- in workers exposed to Benzidine in se epidemiologic investigations greatly ceeded the incidence of this disease in general population.

*,3'-Dichlorobenzidine.* The determiion that 3,3'-Dichlorobenzidine CB) is potentially carcinogenic for nans rests on the determination that B has been shown to be carcinogenic controlled animal studies involving s, mice and hamsters. A clearly de- ed and statistically significant worker pulation exposed to DCB only, in either past or in the present, is difficult to ertain. Existing worker populations ve been either exposed to other listed emical carcinogens in their past work perience or are presently being exposed other suspect carcinogens in addition DCB. Therefore, the case for the man carcinogenicity of DCB must rely extrapolation to humans of the most rtinent animal studies of oncogenesis. The studies by the NCI concerning the uction of tumors, significantly includ- bladder tumors in hamsters, and the dies by Pliss et al. concerning the uction of tumors in mice and rats esent experimental evidence of tumor oduction in three animal species.

Although DCB has been detected in urine of workers receiving a minim of exposure, the metabolism of this bstance is unclear, although it probly differs from that of other carcinoic aromatic amines such as Benzidine d beta-Naphthylamine.

*-Dimethylaminoazobenzene.* Numer- reports concerning carcinogenicity 4-Dimethylaminoazobenzene (DAB) experimental animals have been pubhed. This substance was demonstrated be carcinogenic in rats, dogs, neonatal ce and trout. The similarity in metabsm of various aromatic amines in gs and humans, emphasizes the imtance of the finding that DAB has en demonstrated carginogenic for dogs.

*lpha-Naphthylamine.* The contamition of alpha-Naphthylamine (1-NA) beta-Naphthylamine (2-NA) a potent rcinogen, and mixed occupational exsures involving 1-NA and other aroatic amines has confounded the epiniologic conclusion that 1-NA is carogenic in man. Both 1-NA and 2-NA e readily metabolized to various derivaes, several of which have a demonated carcinogenic potential in experintal animals. The demonstration that metabolite of 1-NA, N-Hydroxy-1phthylamine, possessed a greater carogenic potential than the correspond- 2-NA metabolite, N-Hydroxy-2phthylamine, emphasizes this considation. In addition, the extensive epiniologic study in the dyestuffs indus- conducted by Case failed to eliminate active role for 1-NA as a human bladr carcinogen.

*beta-Naphthylamine.* beta-Naphthylmine (2-NA) was demonstrated to induce cancer of the urinary bladder in dogs, rhesus monkeys and hamsters. Tumors were induced in other organs of rats and mice exposed to 2-NA although attempts at tumor induction in rabbits was unsuccessful. Epidemiologic investigations of worker populations exposed to 2-NA clearly demonstrates that this substance is carcinogenic in humans.

*4-Nitrobiphenyl.* Because of the structural similarity of 4-Aminodiphenyl to 4-Nitrobiphenyl and the experimental evidence for in vivo formation of 4-Aminodiphenyl from 4-Nitrobiphenyl, the epidemiologic investigations published by Melick et al. and by Koss et al. are of special significance. These studies have demonstrated the potential of 4-Aminodiphenyl to induce urinary bladder cancer in humans. The case of the carcinogenicity of 4-Nitrobiphenyl is strongly supported by the induction of urinary bladder cancer in dogs, the evidence that 4-Nitrobiphenyl is metabolized, in vivo, to 4-Aminodiphenyl (a highly carcinogenic aromatic amine), and the possibility that the cases of human urinary bladder cancer attributed by Melick et al. to 4-Aminodiphenyl only, may have been induced by exposure to 4-Nitrobiphenyl as well.

*N-Nitrosodimethylamine.* The carcinogenicity of N-Nitrosodimethylamine (DMN) for the liver and kidney of the rat has been repeatedly demonstrated in experimental studies. In addition, primary tumors of the lungs have been induced in rats administered oral doses of DMN and inhalation of DMN has produced tumors of the nasal area. Other experimental animal investigations have demonstrated the carcinogenicity of DMN for the mouse, the hamster, the guinea pig, the rabbit and several species of fish. In view of this broad spectrum of carcinogenic activity in experimental animals, DMN must be regarded as potentially carcinogenic for man.

*beta-Propiolactone.* The carcinogenicity of beta-Propiolactone (BPL) has been demonstrated in mice by skin application, subcutaneous injection and intraperitoneal injection. Malignant tumors have been induced in rats by subcutaneous injection, intratracheal administration, and intragastric feeding. Skin application to hamsters induced a very high incidence of skin tumors. Although epidemiologic evidence demonstrating BPL to possess a carcinogenic potential for humans is not available, the weight of the experimental animal data indicates that BPL is also a carcinogen in humans.

*bis(Chloromethyl) ether.* Investigations with experimental animals (mice and rats) have demonstrated that bis(chloromethyl)ether (BCME) is a very hazardous carcinogenic substance. Skin application or subcutaneous injection of experimental animals has resulted in malignant lesions at the site of application or injection and in malignant tumors of the lungs. Of significance was the demonstration that 1 ppm or 0.1 ppm of BCME in air, induced lung cancer in mice or rats. Epidemiologic investigations conducted separately by the National Institute for Occupational Safety and Health and others demonstrated that employee exposure to BCME is extremely hazardous with a high probability of lung cancer.

*Chloromethyl Methyl ether.* The results of investigations with experimental animals exposed to commercial grades of Chloromethyl methyl ether (CMME) have been inconclusive regarding the carcinogenicity of this substance because of contamination by small concentrations of the highly carcinogenic bis- derivative-bis(Chloromethyl)ether. However, experimental animal investigations involving chemically purified CMME have demonstrated that this substance possesses a carcinogenic potential.

Epidemiologic investigations reported in 1972 and in 1973 strongly implicated CMME as a human carcinogen, although concomitant exposure to BCME cannot be discounted.

*4,4' - Methylene-bis(2 - chloroaniline).* The results of experimental animal studies involving rats and mice, as reported by three different groups of investigators, have clearly demonstrated a carcinogenic potential for 4,4'-Methylene-bis(2-chloroaniline). The results of two industrial studies involving workers exposed to 4,4'-Methylene - bis(2 - chloroaniline) were not definitive and cannot be relied upon to assess the hazards of occupational exposure to this substance, although one of the studies reported that several exposed workers developed hematuria.

*Ethyleneimine.* The carcinogenic potential of ethyleneimine (EI) has been confirmed by a study conducted by Walpole in 1954 involving rats and one sponsored by the National Cancer Institute involving mice. In the first study, animals developed injection site sarcomas which the investigators attributed to the direct action of Ethyleneimine, and in the second study 80 percent of the animals developed tumors, including more than one-half with hepatomas (which the investigators stated had "malignant potentiality") and almost three-quarters with pulmonary tumors. Although high doses of EI were administered the investigators stated there was no way to predict whether man would be more or less susceptible to tumor induction by EI.

The case for the carcinogenicity of EI, then, rests on the extrapolation to humans of the findings in two separate, controlled animal studies. This position is compatible with that of NIOSH concerning the prior demonstration of carcinogenicity in at least two animal studies.

A major question of occupational carcinogenesis relates to the extrapolation of results of animal experimentation to humans. The basis of numerous objections to the proposals is that, even assuming the validity of animal experiments, such do not furnish sufficient evidence that the substances involved are carcinogenic to humans. Extrapolation of results obtained by animal experimentation is alleged to be vitiated by several considerations: (a) That certain cancers are specific only to some species;

(b) that the conditions of animal experiments are out of proportion to, and not consistent with, conditions prevailing in industrial exposure; and (c) that no cancers have yet been detected in humans exposed to the substances. For those substances whose metabolism is understood, and is similar in both animals and man, the fact that they induce cancers in animals warrants the expectation that they will induce cancers in men. This applies to the substances which cause urinary bladder cancers in animals acting, not directly, but indirectly through the mediation of metabolites formed both in experimental animals and in exposed workers. This is also true of those substances which apparently require no metabolic alteration but attack a particular biologic system (e.g., respiratory tract, alimentary canal) which is similar in both animals and humans.

The objections raise the much broader issue of human exposure to a chemical which is only known to have caused cancers in experimental animals.

It is important to note that some opponents of the regulation of such chemicals do not advocate treating them as if they were harmless with respect to carcinogenic potential. Several employers, for instance insist that such substances must be treated with "care" or "respect," while also insisting that they call for significantly less protection than those substances known to be human carcinogens.

We think it improper to afford less protection to workers when exposed to substances found to be carcinogenic only in experimental animals. Once the carcinogenicity of a substance has been demonstrated in animal experiments, the practical regulatory alternatives are to consider them either non-carcinogenic or carcinogenic to humans, until evidence to the contrary is produced. The first alternative would logically require, not relaxed controls on exposure, but exclusion from regulation. The other alternative logically leads to the treatment of a substance as if it was known to be carcinogenic in man.

We agree with the Director of NIOSH, and the report of the Ad Hoc Committee on the Evaluation of Low Levels of Environmental Chemical Carcinogens to the Surgeon General, U.S. Public Health Service, April 22, 1970, that the second alternative is the responsible and correct one. This decision accords with the work practices of some who object to the proposed regulation. For example, although the Pharmaceutical Manufacturers Association argues for the exclusion of research laboratories from the standard, it states as its ground the fact that employees in Pharmaceutical research are taught to work with all chemicals under the assumption that they are dangerous, unless it is specifically known that they are not.

(3) *The petition, zero tolerance, and permit system.* The petition of Oil, Chemical and Atomic Workers Union (OCAW) and Health Research Group (HRG) for an emergency temporary standard on ten substances proceeds on the assumption that any exposure to any amount of a carcinogenic substance must be prevented. Accordingly, it proposes a standard of zero tolerance permitting no exposure whatsoever. This objective would be accomplished by means of a permit system and frequent monitoring and reporting.

We agree with the Ad Hoc Committee on the Evaluation of Low Levels of Environmental Chemical Carcinogens that a safe level of human exposure to any of the 14 carcinogens cannot be established by application of present knowledge. But we are not prepared to draw from this state of knowledge the conclusion that such levels do not exist. First, it is the professional opinion of many knowledgeable people that as yet undetermined safe levels of exposure possibly do exist. Also, a conclusion that safe levels do not exist seems questionable in view of other studies, some in the area of carcinogenicity which demonstrated that below a certain amount of a single or cumulative dosage, no detectable harm is caused, or if harm is caused, the extent of such harm will be of no practicable importance because the latency period prior to manifestation of harmful effects will be of greater duration than the normal lifespan of man. Secondly, no possible exposure to the carcinogens under any circumstances could only be guaranteed by a total ban on the manufacture, use (even for cancer research), and transportation of the substances. As long as the substances are used, exposure to some amounts may occur because of breakdown of equipment or human error. Accordingly, the intent of the standards is to reduce exposure of workers to any of the listed substances to the maximum extent practicable consistent with continued use.

Numerous objections have challenged the authority for, and the administrative feasibility of, the permit system proposed on July 16, 1973 (38 FR 18902). It is argued, for instance, that the Act requires the promulgation of general standards, in accordance with the procedures prescribed in section 6 of the Act, while the proposed permits would be tailored to particular users, and would be issued by a different procedure.

Another objection argues that a permit system, to be effective, would require authority to stop an operation involving a carcinogen by administrative action, in contravention of the statutory scheme which contemplates judicial determinations resulting in the cessation of an operation.

With regard to feasibility, it is pointed out that a multitude of permits would be required, and that, therefore, the implementation of a permit system would require substantial resources and several years.

It has been made clear that there are numerous uses and processes involving carcinogens. It appears, for instance, that there are 800 to 1800 users of 4,4'-methylene bis(2-chloroaniline) alone. The investigations and evaluations of thousands of work situations involving a carcinogen, and the completion of the procedures, possibly including hearings, for the granting of the permits, would require many years and the diversion of substantial resources, even if available, from other serious occupational safety and health problems.

After considering the administrative and legal aspects of a permit system, as against those of general standards enforced by the use of the current enforcement tools of the Act, the decision has been made not to adopt a permit system.

The requirement in the adopted standards for employers to report the uses of carcinogens and the nature of operations involved, together with incidents of releases of carcinogens, will permit significant administrative surveillance.

(4) *Mixtures.* The proposal for this rulemaking proceeding, like the Emergency Temporary Standard, excludes from the scope of the standard mixtures containing less than specified percentages of the 14 listed substances. The specific figure as a cutoff point derives from the regulations of the Commonwealth of Pennsylvania and England, which also regulate exposure to carcinogens, and apparently have faced the same administrative difficulties confronting OSHA. It is recognized that some of the carcinogens may be used in minute amounts with other substances, or may appear as unintended, undesired by-products or contaminants of processes. Some of the substances are used in minute amounts in cancer research laboratories, and for medical purposes. The College of American Pathologists, for instance, points out that for years pathology laboratories and physicians have used benzidine and/or benzidine dihydrochloride for diagnostic purposes. The American Home Products Corporation calls attention to the use of beta-Propiolactone for the sterilization of vaccines and tissue grafts. Koppers, Inc., requests an exemption in some form for materials, such as coal tar and coal tar products, that contain trace amounts of some carcinogens as by-products or contamination of processes essential to our industrial society. It states that the application of the proposed standard to crude mixtures, such as coal tar and coal tar products, without any exemption, would have the effect of closing down large segments of industry, such as steelmaking, wood preserving, roofing, aluminum reduction, and possibly even power plants.

The adopted standards retain the proposed exclusion of solid or liquid mixtures containing less than 1 percent, by weight or volume, of eight of the carcinogens. Solid or liquid mixtures containing 4-Aminodiphenyl, Benzidine (and its salts), 4-Nitrobiphenyl, beta-Naphthylamine, bis-Chloromethyl ether and Methyl chloromethyl ether are excluded only if they contain less than 0.1 percent of those substances. Finally, an exclusion is provided in the destructive distillation of carbonaceous materials, for alpha-Naphthylamine and beta-Naphthylamine, which may occur in such processes.

The overall purpose of all the exclusions is to avoid substantial obstruction, if not stoppage, of the use of many processes and products which are considered useful in industry and even in cancer research, and about which the record contains very little information. We do not know how many such products and processes there are, nor the availability of substitutes for all of the carcinogens involved, nor the effect of the other components of a mixture on the carcinogenic potentiality of the small amounts of the carcinogen involved. The exclusionary percentage for mixtures containing 4-Aminodiphenyl, Benzidine, 4-Nitrobiphenyl, beta-Naphthylamine, bis-Chloromethyl ether and Methyl chloromethyl ether has been lowered from 1 percent to 0.1 percent because these substances are known to be potent human carcinogens.

The exclusion for the destructive distillation of carbonaceous materials is for the purpose of avoiding the extreme consequences to the segments of the industry using vigorous thermal processes at a time when a separate standard-setting proceeding on coke oven emissions will afford the opportunity for a more in-depth consideration of this whole area (see 38 FR 26207). The exclusion of the mixtures rests, not on a finding that the mixtures are non-carcinogenic, but rather on a decision not to regulate them at this time, on the basis of the record of this proceeding.

(5) *Number of Standards Needed.* Another objection to the proposals is that the standard "lumps together" many different substances with different chemicals and physical properties, different physical states, different biological properties and different uses. There is merit in this objection. Accordingly, 14 standards are adopted, one for each substance listed in the proposal of July 16, 1973.

These standards recognize and provide for different uses and operations involving the regulated carcinogens. Ethyleneimine and beta-Propiolactone are immediately corrosive, and provisions are made in the standards for these materials for deluge showers and eye wash fountains, located near places where exposures might be expected. Principally volatile materials will not be present long enough for routine washing or showering to have effect as a protective measure. Thus, a requirement to wash on each exit, and shower at the end of the day, would not offer any significant protection to employees working in areas where the volatile materials, Methyl chloromethyl ether, bis-Chloromethyl ether, Ethyleneimine and beta-Propiolactone, are present in a closed system or closed system transfer operation. Trace amounts that might be adsorbed onto exposed skin vaporize long before the employee would routinely wash or shower. Wash requirements are retained for these materials in isolated system operations because the closed confinement of glovebox gloves would inhibit vaporization if a leak should occur.

Special provisions are made for premix operations involving 4,4 Methylene-bis (2-chloroaniline) and liquid prepolymer. These premix solutions, frozen or otherwise, are packaged in such a manner and used only after the 4,4'-Methylene-bis(2-chloroaniline) and the prepolymer have started to react. No dust hazard exists and a vapor hazard is unlikely. For this reason, the standard requires only protective clothing such as smocks, coveralls, or long-sleeved shirts and pants, and gloves. This, we believe, will afford adequate protection for these workers.

On the other hand, some of the differences pointed out do not require different treatment. There are basically two strategies of control, regardless of the physical state of a carcinogen. One is to isolate the carcinogen and the other is to isolate the area of possible exposure. In cases of isolated systems, the physical state of a carcinogen may be disregarded for practical purposes. When a system is isolated and fully closed so that the substances cannot escape into the work environment, it does not matter if the substance in it is a solid, liquid, or gas. An isolated system achieved by engineering controls is the preferred approach and the basic approach adopted in the standards. That is, the preferred method of control is engineering control, such as by closed systems, mechanical seals, remote controls, and local exhaust ventilation. This approach most effectively isolates employees from potential contamination.

This is the reason for the ban on open vessel operations. Because of consideration of feasibility, special provisions are made for laboratory hoods and transfer point operations, and additional work practice requirements are made applicable to them.

When protection is afforded by means of personal protective equipment, it is thought best to require body coverage, regardless of the physical state of the substance and its path of travel into the body. The reason for such personal protection is that even if a substance is considered to do harm only when ingested or inhaled, it is prudent to provide protective garments to be discarded after use, so that a worker may not accidentally inhale or ingest contaminants adhering to his clothing or body. This precaution is reasonable, especially since the standards do not require full impervious air-supplied suits. OSHA agrees with the many comments that a full impervious air-supplied suit is cumbersome, while impervious garments with air-supplied hoods are adequate and more comfortable to the workers when used in accordance with the work practice provisions of these standards.

(6) *Research laboratories.* Numerous objections have been made to the proposal for identical treatment of industrial use and laboratory use of the carcinogens. There are essentially three objections: (a) That laboratories use very small amounts of the substances; (b) that work is done by, or under the direction of, highly trained personnel; and (c) that, in the absence of an exemption or other special consideration, the standard as proposed would obstruct, and possibly even prevent much research including cancer research.

These objections are well-taken and special provisions are made applicable to laboratory activities. The provisions are derived from the Minimum Safety Guidelines for Research in Cancer (Part 1, For Research Involving Chemical Carcinogens), prepared in draft form by the Cancer Research Safety Committee of the National Cancer Institute. In addition, it is to be noted that the exclusion provisions for certain mixtures may, by themselves, make a whole standard inapplicable.

Personnel engaged in animal support activities must necessarily handle animals exposed in connection with experiments involving one or more of the carcinogens. Such support activities include the feeding of animals, cleaning of cages and the animal room, and caring for the animals, including weighing operations. Such close animal contact involves potential exposure both to a carcinogen and to metabolites of the carcinogen and therefore requires the more stringent controls for such personnel provided in the standards.

(7) *Signs and labels.* The controversy with regard to signs and labels centers on whether the word "cancer" should be used. We believe that a diluted form of warning will not suffice. We appreciate the concern of employers with the reactions of their employees and the users of their products. But we consider of paramount importance that a worker should be fully apprised and realize the possible risks involved in his occupation. The use of the word "suspect" in the phrase "Cancer-Suspect" follows the revised Emergency Temporary Standard issued July 27, 1973. Coupled with the information and training requirement in the standard, it appears to provide the necessary warning to employees.

(8) *Information and training.* Employers are responsible for providing indoctrination and training to their employees on the nature of the carcinogenic hazards in the establishment, and the precautions to be used when working with or in the presence of the carcinogens. Information on the training and education to be provided to employees is specified in each of the standards for a carcinogenic agent.

(9) *Monitoring.* No provisions for specific techniques or instruments for environmental monitoring are contained in the standards adopted. OSHA has requested NIOSH to develop, on a priority basis, methods for determining qualitative and quantitative amounts of the carcinogens in the workplace.

(10) *Medical surveillance.* Medical surveillance by a physician is required in the standards prior to assignment, at yearly intervals thereafter and whenever known or possible exposure to a carcinogen has occurred. Medical surveillance is considered necessary because of the long latency period inherent in occupational carcinogenesis, since initiation of exposure and induction of cancer are not synchronous events.

Title 29—Labor

CHAPTER XVII—OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION, DEPARTMENT OF LABOR

PART 1910—OCCUPATIONAL SAFETY AND HEALTH STANDARDS

Emergency Temporary Standard for Exposure to Vinyl Chloride

1. *Background.* Vinyl chloride (chloroethene), Chemical Abstracts Service Registry No. 75015, is a synthetic chemical made by oxychlorination of ethylene or by hydrochlorination of acetylene. It is the parent compound of a series of thermoplastic resin polymers and copolymers which are widely used for containers, wrapping tissues, electrical insulation, pipe, conduit and a variety of other products. Vinyl chloride has been made commercially in this country since 1939 and present production is in excess of seven billion pounds per year.

Vinyl chloride (VC) is a gas at ambient temperature and pressure and is a chlorinated hydrocarbon which has moderate liver toxicity. The present standard sets a ceiling value of 500 parts per million (ppm) (29 CFR 1910.93).

On January 22, 1974, the Occupational Safety and Health Administration was informed by the National Institute for Occupational Safety and Health (NIOSH) that the B. F. Goodrich Chemical Company reported that deaths of several of its employees from a rare form of liver cancer may have been occupationally related. As a result of this notification, and after consultation with NIOSH and a joint inspection of the plant by OSHA, NIOSH, and the Kentucky Department of Labor, a fact-finding hearing on possible hazards involved with the manufacture and use of both VC and polyvinyl chloride was announced on January 30, 1974 (39 FR 3874), and held on February 15, 1974.

2. *Carcinogenicity of VC.* Information produced at the hearing demonstrated that exposure of laboratory animals (mostly Sprague-Dawley rats) to VC by inhalation at and below the current OSHA standard of 500 ppm induced tumors, including angiosarcomas of the liver. Professor Cesare Maltoni, of the Instituto di Oncologia, Bologna, Italy, reported on a series of experiments on the effect of exposure of rats, mice, and hamsters to VC at concentrations of 10,000; 6,000; 2,500; 500; 250; and 50 ppm for varying periods of time (TR 43–63). Some of the experiments have been concluded, and others are still ongoing. The experimental results so far reported are that tumors have been observed in groups of animals exposed to VC at concentrations as low as 250 ppm. No tumors have been observed in the group of animals exposed to VC at a concentration of 50 ppm. It also appears so far that the total number of tumors, as well as the numbers of angiosarcomas of the liver, decrease as the concentrations of VC are reduced to 250 ppm. Finally, another experiment by Professor Maltoni is underway involving the exposure of 300 animals to VC at concentrations of 50 ppm, in order to assess in a more definitive way whether that level of exposure produces tumors in animals. Data reported by Torkelson, Oyen and Rowe (American Industrial Hygiene Association J 22:354–361 (1961)) indicate that exposure to VC at concentrations of 50 ppm failed to induce tumors in rats, hamsters, rabbits, and dogs.

The employees of the B. F. Goodrich Chemical Company who died from angiosarcoma of the liver had an average exposure of approximately 19 years to vinyl chloride, at unknown concentrations, and variable exposures to other volatile chemicals. (TR 93). Some employees of Union Carbide Company and Goodyear Company are also reported in a post-hearing comment from NIOSH dated March 11, 1974, to have had exposure to vinyl chloride and to have died from angiosarcoma of the liver. Finally, autopsies of four deceased employees revealed that liver angiosarcoma tumors were histologically indistinguishable from the angiosarcoma tumors observed in Professor Maltoni's experimental animals. It is concluded therefore, that vinyl chloride is carcinogenic for humans.

We therefore conclude that the present standard for VC should be lowered from a ceiling of 500 ppm to a ceiling of 50 ppm for the following reasons:

(a) In light of the evidence referred to above including the Maltoni experiments demonstrating that VC is carcinogenic in animals at 250 ppm, we conclude that VC must be considered carcinogenic in man at the same level;

(b) Although Professor Maltoni did not induce tumors in his experimental animals at an exposure concentration of 50 ppm, these data do not support the concept that occupational exposure of employees to concentrations of 50 ppm throughout their working lifetime would be without detrimental health effects;

(c) The question whether safe levels of exposure to carcinogens exist for humans and, if so, what such levels would be, is the subject of continuing scientific deliberation. In the case of VC, Professor Maltoni did not observe tumors in his animals at exposure concentrations of 50 ppm. In addition, Torkelson, Oyen, and Rowe found that exposure to concentrations of 50 ppm of VC failed to induce tumors in rats, hamsters, rabbits, and dogs. Accordingly, there is insufficient evidence at this time to conclude that VC at concentrations of 50 ppm or below poses a grave danger to humans.

(d) The emergency temporary standard adopted represents a substantial reduction in the permissible level of exposure and, in our practical judgment, is the lowest level that can be complied with immediately; and

(e) This standard will be in effect for a period of no longer than six months, during which time the whole question of possible safe exposure of humans to VC will be reconsidered more fully and in the light of more information, including experiments which are under way at this time (TR 47, 49, 71–74).

3. *Petitions for an emergency temporary standard.* In a telegram to the Assistant Secretary of Labor, received on or about March 14, 1974, the President of the United Rubber Workers International Union urged the establishment of an emergency temporary standard for VC. During the hearing of February 15, 1974, the Industrial Union Department, AFL–CIO, and the United Rubber Workers International Union made a joint petition for an emergency temporary standard for VC (TR 141–148), which was also joined by the Oil, Chemical and Atomic Workers International Union (TR 37). At the same hearing, several participants urged, on the other hand, a regular rulemaking proceeding as the most suitable for the orderly development of relevant information (TR 112, 180).

The petitions for an emergency temporary standard specified in detail the contents of the standard requested. In substance, the request is to issue a comprehensive fully-developed standard based on the recommendations of the Standards Advisory Committee on Carcinogens submitted to the Assistant Secretary of Labor on or about August 27, 1973. The recommendations are far-ranging, and cover special categories of operations, signs and labels, medical surveillance, reporting, etc., including a permit system for the use of a carcinogen.

We agree that an emergency temporary standard is necessary; we cannot say on the basis of the information developed so far that a comprehensive standard, such as the one requested, is either necessary or even desirable. It has been decided to promulgate a standard containing only those essential provisions which are deemed necessary to provide protection to employees from grave danger until a regular rulemaking proceeding in accordance with sections 6 (b) and (c) of the Act can be concluded. The reasons for a decision to establish a ceiling value of 50 ppm have already been stated. A decision on other possible, appropriate provisions is best made after consideration of all relevant data and views that interested persons may submit during the proceeding soon to be initiated.

With respect to arguments in opposition to issuance of an emergency temporary standard, the concern and efforts of several companies participating at the hearing for the protection of their employees are recognized. It may also be that some employers in some plants have fully complied with the interim controls recommended by NIOSH on January 30, 1974. There is, however, reason to believe that employees are currently being exposed to VC at concentrations well above 50 ppm. This was asserted several times at the hearing, and not seriously questioned. Moreover, a report, dated March 1974, of a survey by the staff of the Office of Standards Development, OSHA, of several facilities manufacturing VC and polyvinyl chloride revealed concentrations for some job classifications as high as 229 ppm. Therefore, a regulation is considered necessary to provide, immediately, adequate protection to workers ex-

posed to VC. Also, the eight-hour, time-weighted average standard suggested by several participants at the hearing (see, for instance, TR 178), has been rejected. The March 1974 report of the survey revealed that several kinds of work or operations are of short duration. Loading or unloading of a tank car may require approximately 15 minutes. The cleaning of a reactor may require approximately half an hour. An eight-hour, time-weighted average standard would permit exposure to VC at concentrations of 400 ppm for one hour. Such upward excursions, several times the 50 ppm level, cannot be permitted to occur.

4. *The standard.* The standard set out below contains only the requirements deemed necessary to provide protection before the conclusion of the rulemaking proceeding to be commenced shortly.

Because exposure to VC is hazardous, and because such exposure can occur in the processes of synthesizing or polymerizing of VC or in the handling of VC polymers or copolymers which contain absorbed VC, this standard applies to all such processes and to the handling, reacting, manufacturing, processing, releasing, repackaging, or storage of any of these materials. The monitoring requirements serve two purposes, to trigger into operation a compliance program and to check the effectiveness of the program. Also, engineering controls are favored for compliance, and respirators are intended to provide protection until such controls can be installed or in cases where such controls are not feasible.

Accordingly, by reason of the foregoing and on the basis of the record of the hearing of February 15, 1974, with exhibits, the written submissions received before the hearing pursuant to the notice of the hearing, the post-hearing written submissions by the participants at the hearing, the March 1974 report of a fact-finding survey recommendations received from NIOSH, and the other data referred to herein, it is found (1) that VC at concentrations in excess of 50 ppm is physically harmful and carcinogenic; (2) that exposure to VC at concentrations in excess of a concentration of 50 ppm poses a grave danger to employees; (3) that employees are presently exposed to VC at concentrations in excess of 50 ppm; and (4) that the emergency temporary standard set out below is necessary to provide immediate protection to employees from such danger.

Pursuant to section 6(c) of the Occupational Safety and Health Act of 1970, a proceeding will commence shortly in accordance with section 6(b) of the Act, in which the emergency temporary standard will serve as a proposed rule, together with other subsidiary rules. As soon as possible a draft environmental impact statement will be filed with the President's Council on Environmental Quality, and copies will be provided to other appropriate Federal agencies for their comments.

Pursuant to sections 6(c) and 8(c)(3) of the Williams-Steiger Occupational Safety and Health Act of 1970 (84 Stat. 1596, 1599; (29 U.S.C. 655, 657)), and Secretary of Labor's Order No. 12-71 (36 FR 8754), 29 CFR Part 1910 is amended by adding thereto a new § 1910.93q to read as set forth below. In addition, pursuant to section 4(b)(2) of the Act (84 Stat. 1592; (29 U.S.C. 653)), the standard in the new § 1910.93q is determined to be more effective than the corresponding standards now in Subpart B of Part 1910, in Parts 1915, 1916, 1917, 1918, and 1926 of title 29, Code of Federal Regulations, and in Part 50-204 of Title 41 of the Code of Federal Regulations. Therefore, these corresponding standards are superseded by the new standard in § 1910.93q.

1. In 29 CFR Part 1910, § 1910.93 is amended by deleting from Table G-1 the line: "• • • C Vinyl chloride • • • 500 • • • 1300".

2. Part 1910 of Title 29 of the Code of Federal Regulations is amended by adding thereto a new § 1910.93q to read as follows:

**§ 1910.93q Vinyl chloride.**

(a) *Scope and application.* (1) This section applies to any area or operation in which vinyl chloride (chloroethene), Chemical Abstracts Service Registry Number 75015, is manufactured, reacted, handled, processed, released, repacked, or stored.

(2) This section does not apply to the handling, storage, or other use of vinyl chloride polymers and copolymers in the form of fabricated products.

(b) *Permissible exposure.* The occupational environment shall be controlled so that no employee is exposed to vinyl chloride at a concentration in excess of 50 parts per million (ppm) (127.0 mg/cum).

(c) *Monitoring*—(1) *Initial monitoring.* As soon as possible but not later than April 22, 1974, every employer of an employee working in an area or operation in which vinyl chloride is manufactured, reacted, handled, processed, released, repacked, or stored shall begin monitoring the ambient air of the area to determine whether it contains vinyl chloride in concentrations in excess of 50 ppm.

(2) *Frequency.* Monitoring of a sufficient number of employees so that a representative sample of exposures to vinyl chloride may be determined shall be accomplished not less frequently than weekly until all results for three consecutive weeks are at or below 50 ppm. Thereafter, monitoring shall be conducted not less frequently than monthly so long as the concentrations of vinyl chloride do not exceed 50 ppm. If a monitoring sample reveals vinyl chloride in concentrations in excess of 50 ppm, weekly monitoring shall be resumed until all results for three consecutive weeks are at or below 50 ppm.

(3) *Method of monitoring.* Personnel monitoring shall be accomplished by collecting samples by suitable devices worn by the employee. The samples shall be analyzed by gas chromatography or by any other method which is of equivalent sensitivity. The analytical procedure shall be sensitive to 5 ppm of vinyl chloride in air with an accuracy of ±20 percent for a ten minute air sample.

(4) *Employee observation of monitoring.* Employees working in an area or operation whose ambient air is monitored, or their representatives, shall be given a reasonable opportunity to observe the personnel monitoring required by this section.

(5) *Recordkeeping.* The results of all monitoring shall be recorded in writing. The records shall be retained for at least 5 years and shall be made available for inspection and copying by representatives of the Assistant Secretary of Labor for Occupational Safety and Health and the Director of the National Institute for Occupational Safety and Health (NIOSH).

(6) *Employee access.* Each employee and former employee shall have access to such records of the results of monitoring required by this section as will indicate his own exposure to airborne concentrations of vinyl chloride.

(7) *Employee notification.* Each employer shall promptly notify any employee who has been or is being exposed to vinyl chloride in concentrations in excess of 50 ppm, and shall inform him of the corrective action being taken.

(d) *Compliance.* (1) Whenever any monitoring sample reveals vinyl chloride at a concentration in excess of 50 ppm, or whenever any accident, such as rupture of equipment or spillage, indicates the likelihood of a greater than usual release of vinyl chloride into the ambient air, all employees exposed to such concentrations shall be withdrawn to a safe area and shall not be permitted to reenter the work area unless they wear either Type C continuous flow or pressure demand air supplied respirators or self-contained breathing apparatus.

(2) Work which may reasonably be expected to release vinyl chloride in concentrations in excess of 50 ppm, such as repair, maintenance or cleaning of reactors or other equipment containing vinyl chloride, shall be accomplished only by employees wearing Type C continuous flow or pressure demand air supplied respirators or self-contained breathing apparatus.

(3) In any case covered by paragraphs (d)(1) or (d)(2) of this section, in addition to providing the required respirators, the employer shall examine and analyze the source of the excessive concentrations of vinyl chloride in order to determine feasible engineering or operational controls appropriate to reduce the airborne concentrations to the permissable level. Such controls shall be implemented as quickly as possible.

(4) Periodic tests shall be conducted for equipment leaks and for emissions of vinyl chloride which may result from work practices.

3. In 29 CFR Part 1910, § 1910.19 is revised to read as follows:

**§ 1910.19 Special provisions for air contaminants.**

(a) *Asbestos dust.* Section 1910.93a shall apply to the exposure of every employee to asbestos dust in every employment and place of employment covered by § 1910.12, § 1910.13, § 1910.14, § 1910.15, or § 1910.16, in lieu of any dif-

ferent standard on exposure to asbestos dust which would otherwise be applicable by virtue of any of those sections.

(b) *Vinyl chloride.* Section 1910.93q shall apply to the exposure of every employee to vinyl chloride in every employment and place of employment covered by § 1910.12, § 1910.13, § 1910.14, § 1910.15, or § 1910.16, in lieu of any different standard on exposure to vinyl chloride which would otherwise be applicable by virtue of any of those sections.

*Effective date.* These amendments shall become effective on April 5, 1974.

(Secs. 4, 6, and 8, 84 Stat. 1592, 1596, 1599 (29 U.S.C. 653, 655, 657); Secretary of Labor's Order No. 12-71, 36 FR 8754.)

Signed at Washington, DC., this 2d day of April 1974.

JOHN STENDER,
*Assistant Secretary of Labor.*

[FR Doc.74-7890 Filed 4-4-74;8:45 am]

## Title 32A—National Defense, Appendix

## CHAPTER X—OFFICE OF OIL AND GAS, DEPARTMENT OF THE INTERIOR

[Oil Import Reg. 1 (Rev. 5), Amdt. 65]

## OIL IMPORT REG. 1—OIL IMPORT REGULATIONS

### Canadian Imports

There appeared in the FEDERAL REGISTER on February 11, 1974 (39 FR 5193) a proposal to amend several sections of Oil Import Regulation 1 (Revision 5), as amended. Amendment 64 to Oil Import Regulation 1 (Revision 5) made the changes related to the proposed rulemaking for all sections except for sections 29 and 33, both of which pertain to Canadian imports. Publication of amendment of sections 29 and 33 was deferred until discussions could be held with the Canadian government to determine their export policy. Those discussions have been concluded. The Canadian government plans to continue to control exports along the lines of their present controls for at least through September 1974 at which time the method of control may be modified significantly. Accordingly, interested parties should note that, although sections 29 and 33 are written to provide allocations for the entire allocation period May 1, 1974 through April 30, 1975, licenses will only be issued initially for one half of the May 1, 1974 through April 30, 1975 allocation period and the licenses will only be valid for a six month period unless extended by the Director. This procedure will provide for needed flexibility should the Canadian export policy change to the extent that it is necessary to further modify the affected sections of the Oil Import Regulation to conform to such changes.

As stated in the preamble to Amendment 64 the three tier system proposed for making allocations under section 29 did not receive complete acceptance. Also, the proposed change to section 29 was predicated on a continuation of the Federal mandatory crude allocation program in its present form. The Federal Energy Office has now proposed changes to that program. For these reasons it has been decided to retain the historical basis for making allocations of Canadian imports into Districts I-IV. The major change is a provision that requires that a person having an allocation of Canadian imports must process the entire volume of Canadian imports in his own facility.

The changes to section 33 are strictly technical in nature with the exception of the licensing periods referred to above.

This amendment also amends section 3 to provide that entries for consumption of Canadian imports by pipeline under a license issued pursuant to these regulations may be made until midnight of May 15, following the end of the allocation period in which the license authorizing such imports from Canada was issued. This fifteen day overlap is necessary to prevent disruption of pipeline operations at the end of each allocation period.

This amendment 65 becomes effective on April 5, 1974.

WILLIAM A. VOGELY,
*Acting Deputy Assistant Secretary of the Interior.*

Approved

WILLIAM E. SIMON,
*Deputy Secretary of the Treasury.*

A new paragraph (f) is added to section 3 to read as follows:

Sec. 3. Allocation periods.

* * * * *

(f) Notwithstanding the provisions of paragraphs (a) and (c) of this section entries for consumption of Canadian imports by pipeline may be made until midnight of May 15 following expiration of the allocation period in which a license authorizing such imports from Canada was issued.

Section 29 is amended in its entirety to read as follows:

Sec. 29. Canadian Imports—Districts I–IV.

(a) As used in this section, the term "Canadian imports" means imports from Canada of crude oil which has been produced in Canada and unfinished oils which have been derived from crude oil or natural gas produced in Canada and which have been transported into the United States by overland means or over waterways other than ocean waterways.

(b) To be eligible for an allocation of imports under this section, a person must have in Districts I–IV a facility capable of processing Canadian imports.

(c) The Director shall, in accordance with the terms of paragraph (d)(1) of this section, make allocations for the allocation period May 1, 1974 through April 30, 1975 of not to exceed 762,000 average barrels daily of Canadian imports into Districts I–IV.

(d)(1) The Director shall make allocations not subject to license fees of Canadian imports to eligible applicants who received allocations of such imports for the period January 1, 1973 through December 31, 1973, pursuant to section 23 or from the Oil Import Appeals Board under s[illegible], or from both. Each such applica[illegible]e entitled to an allocation [illegible]n imports calculated in acc[illegible] the following formula:

$$\frac{\text{Sum of each eligible applicant's allocation of Canadian imports in 1973 pursuant to section 23 and section 21-expressed in barrels per day}}{\text{Sum of all allocations of Canadian imports in 1973 pursuant to section 23 and section 21-expressed in barrels per day}} \times 762{,}000 \text{ barrels/day}$$

(2) The Director shall issue before May 1, 1974 to each eligible applicant a license equal to one half of the allocation calculated pursuant to subparagraph (1) of this paragraph. Such licenses shall expire on October 31, 1974 unless extended by the Director. The Director shall issue before November 1, 1974 a second license to each eligible applicant equal to the remainder of the allocation calculated pursuant to subparagraph (1) of this paragraph. Such licenses shall expire on April 30, 1975.

(e)(1) Except as provided for in subparagraph (2) of this paragraph a person who imports Canadian imports must process all such imports in his own facility. For the purpose of this paragraph, blending by mechanical means does not constitute processing.

(2)(i) Canadian imports may be exchanged on a barrel for barrel basis for other Canadian imports but each person receiving crude oil or unfinished oils in the exchange must process the crude oil or unfinished oil received in his own facilities. Settlements, credits, monetary, or accounting adjustments reflecting the relative values of the oils involved in the exchange are permissible.

(ii) Canadian imports which are sold to meet the requirements of regulations published by the Federal Energy Office shall not be subject to the provisions of paragraph (e) of this section.

(f) If a person who receives an allocation of Canadian imports under this section fails to import the total quantity of imports specified in the allocation, or if he fails to process all such imports (or Canadian imports received in exchange for such imports) in his facilities before July 1, 1975, or if he fails to meet the requirement of paragraph (e) of this section, then any allocation of Canadian imports for Districts I–IV to which such person may otherwise be entitled for the first allocation period beginning after April 30, 1975 shall be reduced by the Director by the amount of Canadian im-

(c) The Deputy Administrator, Veterinary Services, upon request to him, may approve other identification systems in specific cases and under such conditions as he may prescribe if he determines that such systems provide the necessary information to allow for traceback of the swine to their herd of origin.

Any person who wishes to submit written data, views or arguments concerning the proposed amendment may do so by filing them with Deputy Administrator, Veterinary Services, Animal and Plant Health Inspection Service, U.S. Department of Agriculture, Hyattsville, Maryland 20782 before August 12, 1974.

All written submissions made pursuant to this notice will be made available for public inspection at the Federal Building, 6505 Belcrest Road, Room 870, Hyattsville, Maryland 20782, during regular hours of business (8 a.m. to 4:30 p.m., Monday to Friday, except holidays) in a manner convenient to the public business (7 CFR 1.27(b)).

Comments submitted should bear a reference to the date and page number of this issue in the FEDERAL REGISTER.

Done at Washington, D.C., this 7th day of MAY 1974.

PIERRE A. CHALOUX,
*Acting Deputy Administrator, Veterinary Services, Animal and Plant Health Inspection Service.*

[FR Doc.74-10882 Filed 5-9-74;8:45 am]

## DEPARTMENT OF LABOR

### Occupational Safety and Health Administration

### [ 29 CFR Part 1910 ]

[Docket OSH-36]

### VINYL CHLORIDE

### Proposed Standard

1. *Background.* Vinyl chloride (chloroethene) Chemical Abstracts Service Registry No. 75015, is a synthetic chemical made by oxychlorination of ethylene or by hydrochlorination of acetylene. It is the parent compound of a series of themoplastic resin polymers and copolymers which are widely used for containers, wrapping film, electrical insulation, pipe, conduit, and a variety of other products. Vinyl chloride has been made commercially in this country since 1939 and present production is in excess of seven billion pounds per year.

Vinyl chloride (VC) is a gas at ambient temperature and pressure and is a chlorinated hydrocarbon which has moderate liver toxicity. The previous standard set a ceiling value of 500 parts per million (ppm) (29 CFR 1910.93, Table G-1).

On January 22, 1974, the Occupational Safety and Health Administration (OSHA) was informed by the National Institute for Occupational Safety and Health (NIOSH) that the B. F. Goodrich Chemical Company reported that deaths of several of its employees from a rare liver cancer (angiosarcoma) may have been occupationally related. As a result of this notification and after consultation with the National Institute for Occupational Safety and Health (NIOSH), and a joint inspection of the plant by OSHA, NIOSH, and the Kentucky Department of Labor, a fact-finding hearing on possible hazards involved with the manufacture and use of VC was announced on January 30, 1974 (39 FR 3874) and held on February 15, 1974.

2. *Carcinogenicity of VC.* Information produced at this hearing demonstrated that exposure of laboratory animals (mostly Sprague-Dawley rats) to VC by inhalation at and below the then current OSHA standard of 500 ppm induced tumors, including angiosarcomas of the liver. Professor Cesare Maltoni, of the Instituto di Oncologia, Bologna, Italy, reported on a series of experiments on the effect of exposure of rats, mice, and hamsters to VC at concentrations of 10,000; 6,000; 2,500; 500; 250; and 50 ppm for varying periods of time (TR-43-63). Some of the experiments have been concluded, and others are still ongoing. The experimental results reported were that tumors have been observed in groups of animals exposed to VC at concentrations as low as 250 ppm. No tumors were observed in the group of animals exposed to VC at a concentration of 50 ppm. It also appears that the total number of tumors, as well as the numbers of angiosarcomas of the liver, decreased as the concentrations of VC were reduced to 250 ppm. Another experiment by Professor Maltoni was reported underway involving the exposure of 300 animals to VC at concentrations of 50 ppm, in order to assess in a more definitive way whether that level of exposure produces tumors in animals. Data reported by Torkelson, Oyen and Rowe (American Industrial Hygiene Association J 22: 254-361 (1961)) indicate that exposure to VC at concentrations of 50 ppm failed to induce tumors in rats, hamsters, rabbits, and dogs.

The employees of the B. F. Goodrich Chemical Company who died from angiosarcoma of the liver had an average exposure of approximately 19 years to vinyl chloride, at unknown concentrations, and variable exposures to other volatile chemicals. (TR 93). Some employees of Union Carbide, Firestone Tire and Rubber, and Goodyear were also reported in post-hearing comments to have had exposure to vinyl chloride and to have died from angiosarcoma of the liver. Finally, autopsies of four deceased employees revealed their liver angiosarcoma tumors were histologically indistinguishable from the angiosarcoma tumors observed in Professor Maltoni's experimental animals.

3. *The Emergency Temporary Standard.* On the basis of all information available at that time, and the fact that employees were being exposed at levels around the experimentally observed effect level of 250 ppm, an Emergency Temporary Standard (ETS) was promulgated on April 5, 1974 (39 FR 12342) as 29 CFR 1910.93q. This standard reduced the level from a ceiling of 500 ppm to 50 ppm ceiling. It was expressly recognized that this standard limiting exposures to a 50 ppm level was intended to be a tentative, interim standard, to be in effect no longer than six months, during which time the whole question of possible safe exposure to VC would be reconsidered more fully and in the light of more information, especially results of experiments which were known to be underway at that time.

4. *Additional information.* On April 15, 1974, information and data were presented to representatives of OSHA, NIOSH and the EPA by the Industrial Bio-Test Laboratories, Northbrook, Illinois, concerning results of animal exposure studies with VC, sponsored by the Manufacturing Chemists Association (MCA). Although only preliminary in nature, these results revealed that 2 out of 200 mice exposed to VC concentrations of 50 ppm for 7 hours a day, five days a week, for approximately 7 months, developed angiosarcomas of the liver.

The Industrial Bio-Test Lab data indicate that exposure to VC at 50 ppm may well constitute a serious health hazard to employees. Also, the question of a safe level of exposure for humans cannot be determined at this time, and may continue as a matter for scientific deliberation for many years. We therefore conclude that it is now necessary to propose to change the 50 ppm level established in the ETS to as low a level as can be detected using methodologies outlined in this proposal.

(5) *The proposed permanent standard.* The requirements for a complete standard under section 6(b) of the Occupational Safety and Health Act of 1970 are much more comprehensive than the provisions of the ETS promulgated on April 5. The following proposals are responsive to the additional information on the carcinogenicity of VC, and the requirements of the Act.

A. *Level of exposure.* The proposed standard for employee exposure is set at no detectable level, as determined by a sampling and analytical method capable of detecting vinyl chloride at concentrations of 1 ppm with an accuracy of 1 ppm±50 percent. Although more sensitive methods may be available now or in the future, the methodological sensitivity proposed appears to be the most feasible and generally available. A method of 1 ppm sensitivity has been recommended to OSHA by NIOSH. To minimize the number of persons at risk, a requirement would be established for regulating areas where vinyl chloride is manufactured, reacted, stored, handled, released, repackaged, or used, including operations with polyvinyl chloride containing detectable levels of vinyl chloride. Access to the areas would be limited to authorized employees.

B. *Monitoring.* A program of monitoring would be required to establish whether there are detectable levels in regulated areas and to permit determination of employee exposures on an individual basis. Provision would also be

made for an opportunity to observe monitoring by employees or their designated representatives, as required by section 8(c)(3) of the Act.

C. *Control methods.* Where detectable levels of VC are monitored, two programs would be triggered; an engineering and work practice program to reduce levels below detectability; and while this is on-going, a respiratory protection program for employees in the regulated area.

Engineering controls and work practices are favored methods of compliance because they tend to avoid contamination of the ambient air in the workplace. Accordingly, it is proposed to require the institution of engineering controls and of workpractice methods as soon as feasible, and to require the use of respirators pending the institution of such controls, to supplement such controls where they are insufficient to reduce concentrations of vinyl chloride below the detectable level, in specified work situations, and in cases of emergency. The proposal for continuous flow and pressure demand types of respirators is based on the recommendations of NIOSH, which has observed leakage through chemical cartridge respirators at high concentrations of VC.

A requirement would also be established for the provision and use of protective clothing for employees in the regulated areas. The protective clothing would minimize skin contact with VC vapor, and would provide some measure of protection from splash of liquid in the event of a spill or rupture of equipment. Food, beverages, and like products would be prohibited in the regulated area.

Written operational and emergency plans would be required, along with employee training in routine and emergency duties. Specific requirements would be established for emergency actions and for routine maintenance and decontamination operations, including vessel entry, which are known to present particular hazards.

The purposes of operational and emergency plans and training are to apprise employees of the hazards to which they may be exposed, of the precautions they must take to avoid such hazards, and to rehearse employees in the procedures they must follow in emergencies.

D. *Medical surveillance.* Comprehensive requirements for employee medical examinations are proposed, including necessary tests. Some additional guidance is included for the convenience of physicians. The proposed requirements have been recommended to OSHA by NIOSH as reasonably appropriate to detect liver dysfunction which may be indicative of, or predisposing to, the development of liver angiosarcomas.

E. *Records and reports.* Records of monitoring, medical examinations, and entry to regulated areas are proposed, with provision for access by appropriate OSHA and NIOSH officials. Specific provisions for employee access to monitoring records are included, as well as the requirement to furnish a copy of a medical record to an employee's physician on the employee's request. Establishments conducting VC operations would be required to identify themselves to OSHA, and to report incidents (accidents) resulting in the release of vinyl chloride.

Accordingly, pursuant to sections 6(b), 6(c), and 8(c) of the Occupational Safety and Health Act of 1970 (84 Stat. 1593, 1596, 1599; 29 U.S.C. 655, 657), Secretary of Labor's Order No. 12-71 (36 FR 8754) and 29 CFR Part 1911, it is hereby proposed to amend 29 CFR Part 1910 by revising § 1910.93q as set forth below.

Written data, views, and arguments concerning the proposals may be mailed to the Docket Officer, Docket OSH-36, Room 230, 1726 M Street, N.W., Occupational Safety and Health Administration, Washington, D.C. 20210, postmarked not later than June 10, 1974.

Pursuant to 29 CFR 1911.11 (b) and (c), interested persons may file objections to the proposals, requesting an informal hearing with respect thereto, in accordance with the following conditions:

(1) The objections must include the name and address of the objector;

(2) The objections must be postmarked on or before June 10, 1974;

(3) The objections must specify the provisions of the proposed rule to which objection is taken, and must state the grounds therefor;

(4) Each objection must be separately stated and numbered; and

(5) The objections must be accompanied by a summary of the evidence proposed to be adduced at the requested hearing.

As revised, § 1910.93q would read as follows:

§ 1910.93q Vinyl Chloride.

(a) *Scope and application.* (1) This section applies to any area or operation in which vinyl chloride (chloroethene), Chemical Abstracts Service Registry No. 75015, is manufactured, reacted, released, repackaged, stored, or used, including areas and operations involving polyvinyl chloride where detectable levels of vinyl chloride are released.

(2) This section does not apply to the handling or use of fabricated products made entirely or in part of polyvinyl chloride.

(b) *Definitions.* (1) "Assistant Secretary" means the Assistant Secretary of Labor for Occupational Safety and Health, U.S. Department of Labor or his designee.

(2) "Authorized employee" means an employee whose duties require him to be in the regulated area and who has been specifically assigned by the employer; and any employee who enters such an area as a designated representative of employees to exercise an opportunity to observe monitoring and measuring of vinyl chloride.

(3) "Closed container" means any container which prevents the release of vinyl chloride to the environment.

(4) "Contaminated" means capable of releasing a detectable level of vinyl chloride.

(5) "Decontamination" means reduction of vinyl chloride concentrations to less than detectable levels.

(6) "Detectable level" means an airborne concentration of vinyl chloride measurable by a sampling and analytical method capable of measuring concentrations of 1 ppm, with an accuracy of 1 ppm±50 percent.

(7) "Director" means the Director, National Institute for Occupational Safety and Health, or any person directed by him or the Secretary of Health, Education, and Welfare to act for the Director.

(8) "Emergency" means an unforseen circumstance or set of circumstances, resulting in the release of vinyl chloride into areas occupied by employees.

(9) "Exposure" means actual contact with vinyl chloride when unprotected by required personal protective equipment and clothing.

(10) "Fabricated product" means a finished product or part of such product, made of polyvinyl chloride, entirely or in part, including semifinished products such as film, sheet, block, bar, or extrusion stock.

(11) "OSHA Area Director" means the Director for the Occupational Safety and Health Administration Area Office having jurisdiction over the geographic area in which the establishment is located.

(12) "Polyvinyl chloride" means polyvinyl chloride homopolymer or copolymer before such is converted to a fabricated product.

(13) "Protective clothing" means clothing protective against vinyl chloride.

(14) "Vinyl chloride" means vinyl chloride monomer.

(15) "Waste resin" means any resin or other reaction products removed in the cleaning of equipment, such as vessels and piping.

(c) *Reference.* College of American Pathologists, 230 N. Michigan Ave., Chicago, Illinois 60601.

(d) *Regulated areas.* (1) A regulated area shall be established where (i) vinyl chloride is manufactured, reacted, released, repackaged, stored, or used; or (ii) polyvinyl chloride capable of releasing detectable levels of vinyl chloride is manufactured, reacted, released, repackaged, stored, or used.

(2) Access to regulated areas shall be limited to authorized employees.

(3) A daily roster of employees entering regulated areas shall be made and maintained. The rosters, or summaries thereof, shall be kept for at least 20 years.

(e) *Monitoring.* (1) Every regulated area shall be monitored for detectable levels of vinyl chloride.

(2) The monitoring shall assure that any exposure may be determined for each authorized employee with a confidence level of 95 percent.

(3) Employees or their designated representatives shall be afforded an opportunity to observe monitoring and measuring required by this paragraph.

(i) Where exercise of an opportunity requires entry to an area where the use

of protective clothing, equipment, facilities, or procedures is required, such clothing, equipment, facilities, and procedures shall be provided to all persons entitled to exercise the opportunity, at no cost to any of them.

(ii) Persons exercising the opportunity shall be instructed regarding:

(A) The toxicity and fire hazard of vinyl chloride; and

(B) The protective steps and measures necessary for their protection.

(iii) Observers shall be permitted, without interference to the persons performing the monitoring and measuring, to:

(A) Observe all steps and procedures related to the collecting, processing, and evaluation of particular monitoring and measurement samples;

(B) Record quantities and results obtained;

(C) Observe the condition of monitoring and measuring equipment;

(D) Receive a demonstration of the calibration and function tests of the monitoring and measuring equipment performed on site; and

(E) Examine instructions and documents related to the procedures and equipment for monitoring and measuring.

(4) Accurate and complete records of all required monitoring shall be made and maintained for not less than 20 years. Such a record shall (i) state the date of such monitoring and the levels determined; and (ii) identify the instruments and methods used.

(f) *Engineering controls and work-practice methods.* (1) Where detectable levels of vinyl chloride are measured, immediate protection shall be provided against exposure to vinyl chloride by the use of engineering controls, workpractice methods, and respirators as follows:

(i) Feasible engineering controls and workpractice methods shall immediately be used to reduce airborne concentrations of vinyl chloride below the detectable level;

(ii) Wherever feasible engineering controls and workpractice methods which can be instituted immediately are not sufficient to reduce concentrations of vinyl chloride below the detectable level, they shall nonetheless be used to reduce the concentrations to the lowest practicable level, and shall be supplemented by means of respirators in accordance with paragraph (g) of this section;

(iii) Wherever no feasible engineering control or workpractice method can be instituted immediately, immediate respiratory protection shall be provided in accordance with paragraph (g) of this section; and

(iv) In any case covered by paragraph (f)(1) (ii) or (iii) of this section, the employer shall also undertake as soon as practicable a program to reduce airborne concentrations of vinyl chloride below the detectable level, or to the greatest extent feasible, solely by means of engineering controls and workpractice methods and as soon as feasible.

(2) There shall be tests made for process or equipment leaks and for emission of vinyl chloride which may result from workpractices. The frequency of these tests shall be such as to insure the integrity of equipment and adherence to proper workpractices.

(g) *Respiratory protection.* (1) A respiratory protection program in accordance with § 1910.134 shall be established and implemented where respirators are required to be used by this section.

(2) Respirators shall be used only in cases of emergency and where required by any other provision of this section. Respirators may not be used in lieu of feasible engineering controls or workpractice methods.

(3) Respirators or combinations of respirators for protection against vinyl chloride shall be selected from among the following:

(i) A positive pressure full facepiece self-contained breathing apparatus;

(ii) A pressure-demand full facepiece self-contained breathing apparatus operating in the pressure-demand mode;

(iii) A combination type "C" pressure-demand full facepiece respirator operating in the pressure-demand mode and a pressure-demand self-contained breathing apparatus operating in the pressure-demand mode; or

(iv) A combination type "C" continuous flow respirator and a pressure-demand self-contained breathing apparatus operating in the pressure-demand mode.

(h) *Protective clothing.* (1) Employees entering regulated areas shall be provided full-body protective clothing, footwear or shoe covers, and gloves, at no cost to them, and required to wear it while in the regulated area.

(2) Where polyvinyl chloride powder containing detectable levels of vinyl chloride is handled, employees shall also be:

(i) Provided and required to wear headcoverings;

(ii) Required to remove all protective clothing at each exit from the regulated area; and

(iii) Required to shower after the last exit of the day.

(3) Clean protective clothing shall be provided whenever contaminated or soiled, but not less frequently than weekly. Contaminated clothing shall be decontaminated before reuse by removal for laundering or disposal.

(i) *Hygiene facilities and practices.* (1) Where employees are required by this section to wear protective clothing and equipment, change rooms shall be provided in accordance with § 1910.141(c).

(2) Where employees are required by this section to shower, shower facilities shall be provided in accordance with § 1910.141(d)(3).

(3) Storage or consumption of food or beverages, storage or use of smoking or non-food chewing products, and the storage or application of cosmetics are prohibited in regulated areas.

(j) *Emergency situations.* (1) A written operational plan for emergency situations shall be developed for each regulated area.

(2) In the event of an emergency, appropriate portions of the plan shall be put into operation.

(i) Hazardous conditions created by the emergency shall be eliminated and the affected area shall be decontaminated prior to the resumption of normal operations.

(ii) Special medical surveillance by a physician shall be instituted within 24-hours for employees present in the affected area at the time of the emergency.

(iii) Where an employee has a known contact with liquid vinyl chloride such employee shall be required to shower as soon as possible, unless contraindicated by physical injuries.

(iv) An incident report on the emergency shall be reported as required in paragraph (q)(2) of this section.

(3) Each authorized employee shall be trained in a program relating to the hazards of vinyl chloride and the precautions for safe use.

(i) The program shall include:

(A) The nature of the fire hazard, and the necessary protective steps;

(B) The nature of the toxic hazard, including local and systemic effects, acute and chronic effects including specifically the carcinogenic hazard;

(C) The specific nature of operations which could result in exposure to vinyl chloride, and necessary protective steps;

(D) The purpose for and application of the medical surveillance program;

(E) The purpose for and application of decontamination practices;

(F) The purpose for and significance of emergency practices and procedures;

(G) The employee's specific role under normal operating or emergency conditions;

(H) Specific information to aid the employee in recognition and evaluation of conditions and situations which may result in the release of vinyl chloride;

(I) The purpose for and application of specific first aid procedures and practices;

(J) A review of this standard at the employee's first training and indoctrination program and annually thereafter.

(ii) All materials relating to the program shall be provided upon request to authorized representatives of the Assistant Secretary and the Director.

(k) *Signs and labels.* (1) Entrances to regulated areas shall be posted with signs bearing the legend:

CANCER-SUSPECT AGENT AREA
AUTHORIZED PERSONNEL ONLY

(2) Areas containing operations covered in paragraph (k)(1)(4) of this section shall be posted with signs bearing the legend:

CANCER-SUSPECT AGENT IN THIS AREA
FULL IMPERVIOUS AIR-SUPPLIED EQUIPMENT REQUIRED
AUTHORIZED PERSONNEL ONLY

(3) Containers of waste or other materials contaminated with vinyl chloride shall be labeled:

VINYL CHLORIDE CONTAMINATED MATERIAL
CANCER-SUSPECT AGENT
DISPOSE OF OR DECONTAMINATE USING AUTHORIZED PRECEDURES

(4) Containers of polyvinyl chloride containing detectable levels of vinyl chloride shall be labeled:

POLYVINYL CHLORIDE
CONTAINS VINYL CHLORIDE
VINYL CHLORIDE IS A
CANCER-SUSPECT AGENT
ABSORBED BY BREATHING AND
THROUGH SKIN

(5) Containers of vinyl chloride shall be labeled:

VINYL CHLORIDE
DANGER
EXTREMELY FLAMMABLE GAS
UNDER PRESSURE
MAY POLYMERIZE WITH
EXPLOSIVE FORCE
POISON
CANCER SUSPECT AGENT AND
ANESTHETIC
ABSORBED BY BREATHING
AND THROUGH SKIN

(6) No statement shall appear on or near any required sign, label or instruction, which contradicts or detracts from the effect of any required warning, information or instruction.

(l) *Maintenance and decontamination.* (1) Emphasis shall be placed upon immediate clean up of spills, periodic inspection, prompt repair of equipment and leaks, and proper handling, storage and disposal or decontamination of materials to prevent airborne contamination and accidental skin contact with vinyl chloride. Waste materials, equipment, and other sources of vinyl chloride in closed containers, may not be placed in areas of excessive temperature or sunlight since build-up of internal pressure may result in rupture of the container, fire or explosion.

(2) Waste resins or other materials contaminated with vinyl chloride shall be placed in closed containers pending disposal or decontamination.

(3) Appropriate procedures shall be developed and implemented for the decontamination or disposal of all such waste material.

(4) In maintenance or repair operations on contaminated—systems or equipment, including vessel entry, employees engaged in such operations shall be (i) provided with and required to wear and use a whole-body air-supplied suit impervious to vinyl chloride, and a respirator in accordance with paragraph (g) of this section; and (ii) required to shower after removing protective equipment.

(5) Protective clothing and equipment shall be clean and dry for each use.

(6) When vessels or piping systems are opened local exhaust ventilation shall be provided to remove the escaping vapor from all occupied areas.

(7) (i) Vessels to be entered shall first be ventilated and monitored so that the concentration of vinyl chloride is reduced to a level within the protection factor capability of the protective equipment.

(ii) When vessels are to be entered, all piping to such vessel shall be:

(A) Opened, blanked and tagged; or

(B) Where welded piping is in use, not less than 2 valves in series, which isolate the vessel from any other connection to such line, must be closed and secured.

(iii) No employee shall enter a vessel, except when another employee properly trained and equipped for entry is present and is observing the employee in the vessel. The observer shall have means for signalling for help in the event the employee experiences problems. Under such conditions, the observer shall signal for help, and shall not enter to assist the employee until another person is present to observe.

(m) *Transportation loading and unloading.* (1) Facilities for the loading and unloading of vinyl chloride to and from containers shall have each transfer line and vapor-equalizing line equipped with vent connections, and shall have an inert gas purging system. Vent and purge effluent shall be returned to a process stream or flared in a safe location.

(2) Procedures shall be developed and implemented for the transfer of vinyl chloride. Written copies of such procedures shall be provided employees engaged in such operations, and such employees shall be fully trained and rehearsed in all procedures.

(3) Employees engaged in transfer operations shall be provided with and required to wear respirators in accordance with paragraph (g) of this section.

(n) *Polymer handling operations.* (1) Containers of polyvinyl chloride releasing detectable levels of vinyl chloride shall be opened and transferred only under local exhaust ventilation which reduces the concentration of vinyl chloride below the detectable level.

(2) Hot operations, such as but not limited to milling, calendering and extruding, which release detectable levels of vinyl chloride, shall be carried on only under local exhaust ventilation which reduces the concentration of vinyl chloride below the detectable level.

(o) *Medical surveillance.* Not later than _____ 1974, a program of medical surveillance shall be instituted, and shall provide each authorized employee with an opportunity for examinations in accordance with this paragraph. All medical examinations and procedures shall be performed by or under the supervision of a licensed Doctor of Medicine (MD) or Doctor of Osteopathy (DO). All medical examinations and tests shall be provided without cost to the employee.

(1) At the time of initial employment, or upon institution of screening, a physical examination shall be performed with specific attention to detecting enlargement of liver or spleen by abdominal palpation.

(2) At the time of initial employment or upon institution of screening, and annually thereafter, a medical history checklist shall be completed by the employee. This list shall include questions concerning:

(i) Alcohol intake;

(ii) Past history of hepatitis;

(iii) Past exposure to potential hepatotoxic agents, including drugs and chemicals;

(iv) Past history of blood transfusions; and

(v) Past history of hospitalizations.

(3) At the time of initial employment, or upon institution of screening, a serum specimen shall be obtained for screening with respect to the following bio-chemical determinations of liver function:

(i) Total bilirubin;

(ii) Alkaline phosphatase;

(iii) Serum glutamic oxalacetic transaminase (SGOT);

(iv) Serum glutamic pyruvic transaminase (SGPT); and

(v) Gamma glustamyl transpeptidase (GGTP).

(4) Additional tests that may optionally be considered for use in screening include:

(i) Lactic dehydrogenase;

(ii) Serum protein determinations;

(iii) Serum protein electrophoresis; and

(iv) Platelet count.

(5) Laboratory analyses for all biological specimens included in medical examinations shall be performed in laboratories accredited by the College of American Pathologists or licensed under 43 CFR Part 74.

(6) If the results of screening required in paragraph (o)(3) of this section are normal, screening shall be repeated:

(i) Every six months for employees who have been employed in vinyl chloride related operations for 10 years or more; and

(ii) Annually for all other employees entering regulated areas.

(7) If one or more liver function tests performed are abnormal, serum testing shall be repeated as soon as possible, preferably within two to four weeks. If no abnormalities are present upon rescreening, serum testing shall be repeated in three months.

(8) If abnormalities persist upon rescreening, the employee shall be withdrawn from areas where contact with vinyl chloride is possible, and an individualized medical workshop shall be instituted. Suggested as initial steps are a complete physical examination and various special procedures such as hepatitis B antigen determination and liver scanning. If liver function abnormalities are determined to be unrelated to liver disease, the employee may be permitted to return to vinyl chloride-related employment, subject to individual medical evaluation.

(9) A complete and accurate record of the results of medical examinations shall be made and maintained for the duration of employment plus five years, or for 20 years, whichever is longer.

(p) *Records.* (1) Records of monitoring and measuring, medical records, and regulated area entry rosters and summaries, shall be made available for examination and copying upon request to authorized representatives of the Assistant Secretary and the Director.

(2) In the event that the employer ceases to do business and there is no successor to receive and retain his records for the prescribed period, these records shall be transmitted by registered mail to the Director, and each employee individually notified in writing of this transfer.

(3) Employees and their designated representatives shall be provided access to examine and copy records of monitoring and measuring.

(4) Former employees shall be provided acces to examine and copy records reflecting their own exposures.

(5) Upon written request of any employee, a copy of the medical record of such employee shall be furnished to a physician designated by the employee in such request.

(q) *Reports.* (1) Not later than _____ the following information shall be reported to the OSHA Area Director. Any change in such information shall be reported to the OSHA Area Director within 15 days of such change.

(i) The address and location of each establishment which has one or more regulated areas; and

(ii) The number of employees in each regulated area during normal operations, including maintenance.

(2) Incidents which result in the release of vinyl chloride into any area where employees may be exposed shall be reported in accordance with this paragraph.

(i) A report of the occurrence of the incident and the facts obtainable at that time including a report on any medical treatment of affected employees shall be made within 24 hours to the OSHA Area Director.

(ii) A written report shall be filed with the OSHA Area Director within 15 calendar days thereafter and shall include:

(A) A specification of the amount of material released;

(B) A description of the area involved and the extent of known and potential employee exposure and area affected;

(C) A report on any medical treatment of affected employees and any medical surveillance program implemented; and

(D) An analysis of the circumstances of the incident, and measures taken or to be taken, with specific completion dates, to avoid further similar releases.

(3) Upon completion of any monitoring and measuring which discloses that any employee has actually been exposed to detectable levels of vinyl chloride, each such employee shall be individually notified in writing. The notice shall:

(i) Be delivered not later than 10 working days after completion of the monitoring and measuring;

(ii) State the actual exposure in terms of concentration and time; and

(iii) State the steps which have been taken, are being taken, and will be taken, with specific completion dates, to terminate the exposure and prevent a recurrence.

(Secs. 6(b), 6(c), and 8(c), 84 Stat. 1593, 1596, 1599 (29 U.S.C. 655, 657); Secretary of Labor's Order No. 12-71 (36 FR 8754))

Signed at Washington, D.C. this 6th day of May, 1974.

JOHN STENDER,
*Assistant Secretary of Labor.*

[FR Doc.74-10748 Filed 5-9-74;8:45 am]

## DEPARTMENT OF TRANSPORTATION

### Federal Aviation Administration

### [ 14 CFR Part 25 ]

[Docket No. 13696; Notice 74-19]

### TRANSPORT CATEGORY AIRPLANES

### Type A Passenger Emergency Exit Capacity

The FAA is considering rule making to revise the passenger seating configuration limit that is applicable to Type A exits on transport category airplanes. Sections 25.807(c) (2) and (3) of the Federal Aviation Regulations (FARs) currently provide that for each pair of Type A exits (consisting of one on each side of the fuselage) the airplane may have a maximum passenger seating configuration of 100.

This advance notice of proposed rule making is being issued in accordance with the FAA's policy for early institution of public proceedings in actions related to rule making. An "advance" notice is issued to invite early public participation in the identification and selection of a course or alternate courses of action with respect to a particular rule making problem.

Interested persons are invited to participate in the rule making by submitting such written data, views, or arguments as they may desire. Communications should identify the regulatory docket or notice number and be submitted in duplicate to: Federal Aviation Administration, Office of the Chief Counsel, Attention: Rules Docket, AGC-24, 800 Independence Avenue, SW., Washington, D.C. 20591. Communications should be received on or before July 9, 1974, to assure proper consideration. All comments submitted will be available, both before and after the closing date for comments, for examination by interested persons.

The regulatory provisions relating to Type A exits that are contained in § 25.807 of the Federal Aviation Regulations were adopted by Amendment 25-15, effective October 24, 1967. That amendment also established the provision, in § 25.803(c), that manufacturers show by demonstration that the maximum seating capacity of an airplane having a capacity of more than 44 passengers can be evacuated to the ground within 90 seconds, under conditions prescribed in the regulation. As discussed in the preamble to Amendment 25-15, the allowable passenger seating limit of 100 that was established for each pair of Type A exists was less than the evacuation capacity that had been demonstrated by test. As a result of receiving data and information tending to indicate that some of the considerations leading to the conservative limitation may no longer be applicable, the FAA has instituted a regulatory study project to reevaluate the limitation. The study will include the factors originally considered in establishing the limitation as well as any other factors found to be pertinent. Those factors originally considered include pertinent evacuation tests and demonstrations, exterior slides, the number, location, and size of aisles and passageways, and evacuation system reliability.

Data available to the FAA on in-service evacuations, slide deployments, and evacuation demonstrations indicate that more than 100 passengers have been evacuated through a Type A exit within 90 seconds. The data further indicate that Type A exit systems may have higher in-service reliability than was anticipated at the time the limitation was established in the regulations. However, the FAA believes it is important to review all relevant data on safety and cost considerations that may be applicable to any proposed change in the Type A exit passenger seating limitation. To this end, the FAA solicits data, views, and arguments from all interested persons on the questions set forth below. Data supporting an answer should be submitted or identified sufficiently that the FAA may obtain or develop it.

1. Do the data available on evacuation tests and in-service incidents that relate to the evacuation capacity of Type A exits under emergency conditions indicate that the 100 passenger limitations may safely be increased?

2. What reliability has been demonstrated for Type A exit systems by service experience and tests?

3. What relationships may be established between reliability and passenger emergency evacuation capability of Type A exits?

4. How would the emergency evacuation capability of Type A exits be affected by specific increases in passenger seating capacity and by specific passenger seating configuration considerations?

5. If there are other factors that should be considered, how should the relevant data be related to the emergency evacuation capability of Type A exits?

6. If the commentator recommends specific passenger capacities for consideration, what economic and safety benefits or penalties would be associated with them?

Issued in Washington, D.C., on May 2, 1974.

C. R. MELUGIN, Jr.,
*Acting Director,*
*Flight Standards Service.*

[FR Doc.74-10787 Filed 5-9-74;8:45 am]

### [ 14 CFR Part 39 ]

[Docket No. 74-NW-4-AD]

### AIRWORTHINESS DIRECTIVES

### Boeing Model 737-100/200 Series Airplanes

The Federal Aviation Administration is considering amending Part 39 of the

# proposed rules

This section of the FEDERAL REGISTER contains notices to the public of the proposed issuance of rules and regulations. The purpose of these notices is to give interested persons an opportunity to participate in the rulemaking prior to the adoption of the final rules.

## DEPARTMENT OF LABOR

### Occupational Safety and Health Administration

[29 CFR Part 1910]

[Docket No. OSH-36]

### VINYL CHLORIDE

### Availability of Economic Impact Study

On May 10, 1974, pursuant to sections 6(b), 6(c), and 8(c) of the Williams-Steiger Occupational Safety and Health Act of 1970 (84 Stat. 1593, 1596, 1599; 29 U.S.C. 655, 657), Secretary of Labor's Order No. 12-71 (36 FR 8754), and 29 CFR Part 1911, a proposed standard concerning occupational exposure to vinyl chloride was published in the FEDERAL REGISTER (39 FR 16896). On June 25-28 and July 8-11, 1974, an informal rulemaking hearing was held on the proposal pursuant to section 6(b)(3) of the Act.

At the close of the hearing, the presiding Administrative Law Judge, Gordon J. Myatt, ruled, in accordance with the authority granted him under 29 CFR 1911.16(g), that the record would remain open until August 23, 1974 for the receipt of general comments and an additional period after that date solely for the submission of written comments on the economic impact study being conducted for OSHA by an independent consultant. The study, which examines the economic and technological feasibility of compliance with the proposed standard in the monomer, polymer and copolymer producing industries, is now available for examination and copying in Room 230, 1726 M Street, NW., Occupational Safety and Health Administration, Washington, D.C. 20210. All comments regarding the economic impact study should be mailed to the Docket Officer, Docket OSH-36, at the above address, and must be postmarked no later than September 6, 1974.

Signed at Washington, D.C. this 22nd day of August, 1974.

JOHN STENDER,
*Assistant Secretary of Labor.*

[FR Doc.74-19767 Filed 8-23-74;8:45 am]

## DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

### Food and Drug Administration

[21 CFR Parts 1 and 314]

### REQUIREMENTS FOR DISPENSING CONTAINERS FOR PRESCRIPTION DRUGS

### Notice of Proposed Rulemaking

Recent trends towards the use of dispensing containers made of materials other than glass and the increased use of films, laminates, papers, and foils present new problems to the pharmacist in dispensing a drug product because of the different properties of these materials. Many drug products are subject to decomposition or deterioration if not properly protected from heat, light, and exposure to air or moisture; therefore it is necessary that the container used by the pharmacist in dispensing the drug product to the patient be adequate to maintain the product's original identity, strength, quality, and purity.

The monographs for many of the drug products recognized in the official compendia include requirements for the use of specific types of dispensing containers, e.g., light-resistant container, tight container, well-closed container. These requirements for the use of specified containers apply to products when dispensed by the pharmacist unless otherwise indicated in the monograph. In the absence of official tests and specifications, the pharmacist often has little or no information available to assist him in selecting a suitable container.

The Food and Drug Administration has met with representatives of the National Formulary (N.F.) and the United States Pharmacopeia (U.S.P.) to develop official standards and test procedures for determining that dispensing containers for prescription drugs meet the requirements for specified types of containers as defined in the official compendia. The N.F. on January 2, 1974, proposed the first such official standard for tightness of drug containers. The proposal includes a test procedure as well as suggested limits for "tight containers" and "well-closed containers" as defined by the compendia. The proposed requirements are applicable to multiple-unit containers, i.e., a vial or other drug container permitting withdrawal of successive doses or portions of the contents. It is anticipated that implementation of the standards will be made simultaneously by the N.F. and the U.S.P.

The Commissioner of Food and Drugs has determined that the pharmacist must have information readily available to him as to the type of dispensing container which must be used to maintain a drug product's original identity, strength, quality, and purity. Chemically identical drugs, because of formulation differences, may have different requirements for packaging and storage that may not be apparent without extensive testing. It is not reasonable to expect the pharmacist to test each and every drug product to determine the type of container that must be used to maintain the identity, strength, quality, and purity of the product after it has been dispensed to the patient. The Commissioner is of the opinion that the manufacturer of the drug product is the person most able to supply the necessary information as to what constitutes a suitable container for dispensing his drug product.

Therefore, the Commissioner proposes to require that the manufacturer include, as part of the prescription drug product label, information, directed to the pharmacist, as to the type of container to be used in dispensing the drug product to the patient. This information may be in terms of specific materials, containers, or in terms included in the official compendia to define suitable containers, e.g., "Preserve in a tight container". In the case of containers too small or otherwise unable to accommodate a label with sufficient space to bear this information, but which are packaged within an outer container from which they are removed for dispensing or use, this information may be contained in other labeling on or within the package from which it is to be dispensed.

The Commissioner proposes that the requirements of this proposal be implemented so as to be concurrent with simultaneous implementation of container standards by the N.F. and the U.S.P.

Therefore, pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 503, 505, 507, 701, 52 Stat. 1050-53, 1055-56, as amended, 59 Stat. 463, as amended; 21 U.S.C. 352, 353, 355, 357, 371) and the Public Health Service Act (sec. 351, 58 Stat. 702; 42 U.S.C. 262), and under authority delegated to him (21 CFR 2.120), the Commissioner of Food and Drugs proposes to amend Parts 1 and 314 as follows:

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### PART 1—REGULATIONS FOR THE ENFORCEMENT OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT AND THE FAIR PACKAGING AND LABELING ACT

1. In § 1.106 by revising paragraph (b)(2)(vi), adding a new paragraph (b)(2)(vii) and by revising the undesignated material at the end of paragraph (b)(2) to read as follows:

§ 1.106 Drugs and devices; directions for use.

* * * * * *

(b) * * *

(2) * * *

(vi) An identifying lot or control number from which it is possible to determine the complete manufacturing history of the package of the drug; and

(vii) A statement directed to the pharmacist specifying the type of container to be used in dispensing the drug prod-

The proposed amendment is presented below:

Part A of Schedule II to DPS Regulation 1 is hereby amended to read as follows:

PART A

The following items under the jurisdiction of BDC are presently not subject to any ratings issued by or under authority of BDC (but are subject to directives issued by or under authority of BDC) and therefore such ratings shall not be effective to obtain any of them: [1]

Communications services.
Crushed stone.
Gravel.
Sand.
Scrap.
Slag.
Steam heat, central.
Waste paper.

* * * * *

(Defense Production Act of 1950, as amended (64 Stat. 816; 50 U.S.C. App. 2061 et seq.); Executive Order 10480, as amended, 18 FR 4939, 6201, 19 FR 3807, 7249, 21 FR 1673, 23 FR 5061, 6971, 24 FR 3779, 27 FR 9683, 11447, 3 CFR 1949–1953 Comp., p. 919; Executive Order 11725, 38 FR 17175; DMO 8400.1, 32A CFR Part 15; Department of Commerce Organization Order 10–3, 38 FR 33624, and 40–1, 39 FR 1871; Department of Commerce, Domestic and International Business Administration Organization and Function Orders 41–1, as amended, 39 FR 2780, 39 FR 18490, 45–1, 39 FR 18488, and 45–2, 39 FR 18489)

Dated: September 10, 1974.

DOMESTIC AND INTERSTATE BUSINESS ADMINISTRATION, BUREAU OF DOMESTIC COMMERCE,
SAMUEL B. SHERWIN,
*Deputy Assistant Secretary for Domestic Commerce.*

[FR Doc.74-21181 Filed 9-12-74;8:45 am]

[1] The following delegations and agreements, as the same may from time to time be amended, revoked, or superseded, further delineate jurisdictional responsibilities for the exercise of priorities and allocations powers:

(1) Memorandum of Agreement between the Department of the Interior and the Department of Commerce with respect to the production and/or distribution of designated products and equipment, including chemicals, associated with the output of petroleum and gas, effective October 30, 1973 (38 FR 30896).

(2) Defense Solid Fuels Administration (DSFA) Delegation 1 to the Secretary of Commerce with respect to the distribution of coal chemicals produced as by-products of coke made from coal, effective May 15, 1951 (16 FR 4590). The DSFA was abolished in 1954 and its responsibilities within the Department of the Interior have been transferred to the Office of the Assistant Secretary for Energy and Minerals, Department of the Interior.

(3) Delegation of Authority from the Secretary of Commerce to the Secretary of the Interior of priorities and allocations powers with respect to certain minerals facilities and materials, effective January 26, 1967 (32 FR 2462).

(4) Memorandum of Agreement between the Department of Agriculture and the Department of Commerce with respect to the scope of allocation and priority responsibilities in connection with foods which have industrial uses, effective December 5, 1973 (38 FR 33504).

(5) Memorandum of Understanding and Agreement between the Agricultural Stabilization and Conservation Service, Department of Agriculture, and the Bureau of Competitive Assessment and Business Policy, Department of Commerce, with respect to the scope of the term "farm equipment," effective December 5, 1973 (38 FR 33506). The responsibilities of the Bureau of Competitive Assessment and Business Policy have been transferred to the Bureau of Domestic Commerce (BDC), Department of Commerce.

## DEPARTMENT OF LABOR

### Occupational Safety and Health Administration

[ 29 CFR Part 1910 ]

[Docket No. OSH-36]

### VINYL CHLORIDE

### Availability of Final Economic Impact Study

On May 10, 1974, pursuant to sections 6(b), 6(c), and 8(c) of the Williams-Steiger Occupational Safety and Health Act of 1970 (84 Stat. 1593, 1596, 1599 (29 U.S.C. 655, 657)) Secretary of Labor's Order No. 12–71 (36 FR 8754), and 29 CFR 1911, a proposed standard concerning occupational exposure to vinyl chloride was published in the FEDERAL REGISTER (39 FR 16896). On June 25–28 and July 8–11, 1974, an informal rulemaking hearing was held on the proposal pursuant to section 6(b)(3) of the Act.

At the close of the hearing, the presiding Administrative Law Judge, Gordon J. Myatt, ruled, in accordance with the authority granted him under 29 CFR 1911.16(g), that the record would remain open until August 23, 1974 for the receipt of general comments and an additional period after that date solely for the submission of written comments on the economic impact study being conducted for OSHA by an independent consultant.

On August 26, 1974, a notice was published in the FEDERAL REGISTER (39 FR 30844) announcing the availability of the preliminary report, which examines the economic and technological feasibility of compliance with the proposed standard in the monomer, polymer and copolymer producing industries, and inviting comments to be submitted no later than September 6, 1974.

Several persons requested additional time to comment on the preliminary report and also asked for an opportunity to comment on the final economic impact study when available. Since certain portions to be included in the final report were not contained in the preliminary report, the request for additional time to comment on the preliminary report and for an opportunity to comment on the final report is granted.

The final economic impact report will be available for examination and copying beginning at 10 a.m. on September 16, 1974, in Room 230, 1726 M Street NW., Occupational Safety and Health Administration, Washington, D.C. 20210. This report, although labeled "final draft" because the independent consultant may subsequently make minor editorial corrections, will be treated as the final economic impact report for purposes of this rulemaking proceeding.

All comments regarding the preliminary and final economic impact study should be mailed to the Docket Officer, Docket OSH–36, at the above address, and must be received no later than September 25, 1974.

Signed at Washington, D.C., this 12th day of September 1974.

JOHN STENDER,
*Assistant Secretary of Labor.*

[F.Doc.74-21398 Filed 9-12-74;10:42 am]

## DEPARTMENT OF TRANSPORTATION

### Federal Aviation Administration

[ 14 CFR Part 71 ]

[Airspace Docket No. 74–GL–30]

### TRANSITION AREA

### Proposed Designation

The Federal Aviation Administration is considering amending Part 71 of the Federal Aviation Regulations so as to designate a transition area at the White County Airport, Monticello, Indiana.

Interested persons may participate in the proposed rule making by submitting such written data, views or arguments as they may desire. Communications should be submitted in triplicate to the Director, Great Lakes Region, Attention: Chief, Air Traffic Division, Federal Aviation Administration, 2300 East Devon Avenue, Des Plaines, Illinois 60018. All communications received on or before October 15, 1974, will be considered before action is taken on the proposed amendment. No public hearing is contemplated at this time, but arrangements for informal conferences with Federal Aviation Administration officials may be made by contacting the Regional Air Traffic Division Chief. Any data, views or arguments presented during such conferences must also be submitted in writing in accordance with this notice in order to become a part of the record for consideration. The proposal contained in this notice may be changed in the light of comments received.

A public docket will be available for examination by interested persons in the Office of the Regional Counsel, Federal Aviation Administration, 2300 East Devon Avenue, Des Plaines, Illinois.

A standard instrument approach procedure has been developed for the White County Airport, Monticello, Indiana. Consequently, it is necessary to provide controlled airspace protection for aircraft executing this new approach procedure by designating a transition area at Monticello, Indiana.

In consideration of the foregoing, the Federal Aviation Administration proposes to amend Part 71 of the Federal

PROFESSOR CESARE MALTONI
DIRECTOR, INSTITUTE OF ONCOLOGY
UNIVERSITY OF BOLOGNA
BOLOGNA, ITALY

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THE OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION WILL HOLD A PUBLIC HEARING ON PERMANENT STANDARD FOR VINYL CHLORIDE EXPOSURE ON JUNE 25. TO HAVE AS COMPLETE A RECORD AS POSSIBLE, WE WOULD APPRECIATE A STATEMENT OF YOUR FINDINGS TO DATE, PARTICULARLY ON EXPOSURES AT OR BELOW 50 PPM. REQUEST YOU CABLE DATA AND COMMENTS WHATEVER LENGTH AT OUR EXPENSE. WOULD APPRECIATE RESPONSE NOT LATER THAN JUNE 18 OR 19.

JOHN H. STENDER

ASSISTANT SECRETARY OF LABOR FOR OCCUPATIONAL SAFETY AND HEALTH.

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MR JOHN H STENDER ASSITANT SEVRETARY PSHA
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# INDUSTRIAL HYGIENE SURVEY REPORT ON VINYL CHLORIDE AND POLYVINYL CHLORIDE MANUFACTURING FACILITIES

BY

DIVISION OF HEALTH STANDARDS

OFFICE OF STANDARDS DEVELOPMENT

MARCH 1974

## SUMMARY

1. Five vinyl chloride monomer (VCM) and two polyvinyl chloride (PVC) manufacturing facilities in the New Orleans - Baton Rouge area have been visited by the staff of the Office of Standards Development during a fact-finding survey.

2. The PVC manufacturers have a more serious problem of VCM exposure than the VCM producers because most of the polymerization process equipment are in enclosed areas and ventilation is inadequate.

3. Leaks from the process equipment, vessel entry, VCM tank car loading, unloading, and process sampling, PVC reactor cleaning and compounding and packaging are the major potential sources of VCM exposure found during this survey.

4. Engineering technology for the control of VCM exposure is available and has been implemented by the industry.

5. The observed practices relative to equipment maintenance, monitoring medical examination and surveillance and training are considered to be inadequate to control the employee's exposure to vinyl chloride.

6. The fact-finding survey was found to be very useful in the development of proposed rulemaking of health standards.

# INDUSTRIAL HYGIENE SURVEY REPORT ON VINYL CHLORIDE MANUFACTURING AND POLYMERIZATION FACILITIES

## Introduction

A fact-finding survey of several vinyl chloride (VCM) and polyvinyl chloride (PVC) manufacturing facilities has been conducted by the staff of the Office of Standards Development during the week of March 11. Five VCM Plants and two PVC Plants in the New Orleans and Baton Rouge area were visited during this survey. A list of all plants is presented in Table 1.

## Process

The VCM is either produced by the direct chlorination or oxychlorination of ethylene to ethylene dichloride (EDC) and pyrolysis of EDC to VCM or by the reaction between acetylene and hydrogen chloride. The crude VCM is purified by distillation to yield a product having purity of 99.99%.

The PVC is produced by either wet or dry polymerization process. The wet process is carried out by reacting VCM in aqueous solution containing dispersing or emulsifying agents and catalyst. The dry process produces PVC by direct reaction between VCM and catalyst in a two-stage reactor. The unreacted VCM is separated from the PVC and the raw PVC is ground to desirable size. Block diagrams of various processes are presented in Figure 1 through 4.

## Potential Area of VCM Exposure and Its Control

Based on observations of this survey the areas where exposure to VCM is likely in a VCM plant during normal operations are:

1. Sampling and analysis of VCM for quality control.
2. Loading of VCM for shipping.
3. Entry of VCM containing vessels for maintenance and repair work.
4. Leak of VCM in the process area.

The areas of VCM exposure in a PVC plant can be summarized as the following:

1. Unloading of incoming VCM.
2. Reactor cleaning.
3. Entry of VCM containing vessels for maintenance and repair work.
4. Entry of PVC storage silos.
5. Compounding of PVC into molding powder.
6. Shipping or packaging of PVC.
7. Leak of VCM in the process area.

The VCM plant is operated around the clock and usually five or less employees are worked on each shift. One or two of these employees have to stay outside for one or two hours per shift to take samples, check gages and handle minor maintenance or repair work. About ten VCM samples are collected per shift by one employee. The VCM is collected in a sampling bomb with the time of collection being about one minute. The sampling port can be modified to reduce the exposure of VCM during such operation.

Loading or unloading of VCM is another area of possible VCM exposure. Most loading is done on day shift only and the employee is loading eight or less tank cars at one time. Each loading operation takes about ten minutes. However, if more than one tank car is being loaded at one time the employee may spend as much as six hours on the loading deck every day. One company official claimed that they are installing a system to reduce the emission of VCM during loading. Since the loading deck is located in open space and ventilation is good and if the emission control system is installed and the employee is standing at the upwind director with gloves and face shield, the exposure to VCM is insignificant unless the wind is strong.

The reactor cleaning is probably the area where VCM exposure is highest among VCM and PVC plants. The manufacturing of the PVC is still a batch process and the reaction time is about eight hours. The agitator and the bottom part of a wet process reactor is cleaned after two or three batches were made. The whole reactor of the dry process is

cleaned after each batch was made. The average cleaning time is 30 minutes and usually two employees are performing the task. The dry process reactor is cleaned by using scraper and chisel under local exhaust ventilation. It is a dusty operation and no personal protective equipment of any kind is being used. A filter head which separates unreacted VCM from the PVC is cleaned by compressed air. The operator also uses compressed air to blow dust off his body. The cleaning should be performed by vacuuming or by using scraper equipped with local exhaust ventilation. In addition, the operator should wear coveralls, face shield and gloves with or without supplied air respirator depending on the residual concentration of VCM in the reactor. After the reactants and products have been removed from a wet process reactor vessel, it is filled with water and rinsed one time before cleaning. The cleaning is under local exhaust ventilation. Chisel and scraper are also used for cleaning of this type of reactor. Since the reactor surface is wet, dust exposure is not a problem. However, the exposure to VCM may be likely because cold water rinse is not effective to remove the residual VCM absorbed on the walls of the reactor and steam purging is preferred. No test for VCM concentration in the reactor was made prior to entry. It is a good practice to require the use of supplied air respirator for any reactor cleaning work.

Most employers indicated that they have established procedures for vessel entry and in some companies a permit is required prior to initiation of such operations. It is questionable whether these procedures are enforced, especially regarding VCM exposure A requirement containing details regarding entry of VCM containing vessel for maintenance or repair work should be included in the proposed standard.

There is no information available to date regarding the desorption of VCM from the surfaces of the PVC particles during storage and handling. However, it is preferable to establish a procedure for the entry of PVC storage silos and require local exhaust ventilation systems be installed in all PVC compounding and packaging and loading operations where PVC dust can be released. Although the manufacturing of VCM and PVC is under pressure in a closed system, exposure to VCM is unlikely during normal operation. However, inadequate maintenance and wear of packings and seals of process equipment can results in leaks of VCM.

Nearly all the VCM exposures are outdoors in the VCM plants while most PVC manufacturing operations except in the deep south and west coast where winter climate is mild, are enclosed. The exposure of VCM from equipment leaks can be significant in a PVC plant. We found that most

of the plants do not have maintenance crews on all three shifts and preventive maintenance program is inadequate or non-existent. We should ask the employer to implement a maintenance program to insure that the leakage of VCM is unlikely during normal operations. An equipment check list should be prepared and the frequency of inspection should be based on the probability of failure or malfunctioning of equipment, piping or fittings. The equipment maintenance and repair record should be included in the OSHA record keeping requirements.

The VCM samples collected in the bombs are analyzed by gas chromatography in a quality control laboratory. If the bomb is stored in an exhaust hood with good ventilation and the sample is withdrawn from the hood, no exposure of VCM is expected during such operations.

## Monitoring

Before the outbreak of liver cancers in the Goodrich PVC plant, the VCM was considered a fire hazard and less precise sampling and analytical methods were used for monitoring. This still appears to be the case from the observations gathered on this survey. We obtained some monitoring data from several VCM plants. Only one PVC manufacturer promised us to send us monitoring data on PVC operations. Another PVC plant uses a combustible vapor tester for monitoring VCM exposure and this type monitoring is neither accurate, specific nor sensitive to low concentrations of VCM.

Gas chromatograph (GC) appeared to be a common instrument used for the analysis of VCM. The VCM is either collected as grab or time-weighted-average (TWA) samples in gas-tight syringes, plastic bags or activated charcoal tubes.

By reviewing the monitoring data submitted by two VCM plants (Table II & III) though the data is limited, however, it does indicate that VCM loader, process sample man and maintenance personnel are most likely exposed to higher levels of VCM than other employees in these plants. The method of control of VCM exposure for these employees are discussed in the previous section.

There is wide difference between the sampling method and analytical techniques for VCM. Standardized sampling and analytical procedures should be established for the monitoring of VCM. This may be obtained through NIOSH. Most plants indicated that they are acquiring fixed continuous monitoring stations and more sophisticated portable monitoring for VCM in their facilities. A guideline should be laid out to get the maximum benefit for the use of such instruments.

VCM can be detected by the GC techniques in the order of 1 ppm. The detectable range of two most promising portable direct reading VCM detector, the Century Organic Vapor Analyzer (OVA) and the Wilks Miran infrared spectrophotometer (MIRAN) are in the order of 1 ppm. The accuracy of these instruments at such low concentration may be ±50%. The accuracy of GC is dependent on the preparation and calibration of the standard. The reliability of a prepared standard at 1 ppm may also pose a problem. A 2 ppm concentration may be the lowest limit at which we can have reasonable confidence on these instruments.

The required method of monitoring is dependent on the permissible limit on the proposed standard. If a limit is set, the VCM exposure for each job classification should be monitored on a TWA basis. Personal breathing samples should be collected on a sampling device having a collection efficiency of at least 95%. Sufficient number of area samples should also be collected to pin point high exposure areas for the implementation of control measures. The sensors of a continuous VCM monitoring system can be located at high exposure areas of VCM. The initial monitoring of the workplace should take abnormal operating conditions such as hot weather into consideration and monitoring should be repeated on a periodic basis or after process modifications and repairs.

If no exposure limit is being proposed, the initial monitoring is still required for the implementation of engineering controls. The use of direct reading and continuous monitoring instruments are more imperative since no leaks can be tolerated under such circumstances. The monitoring should be conducted on a daily basis at predetermined sampling points.

## Medical

All plants have preplacement physical examination programs. However, periodic physical examination is not a common practice. Two of the six plants have a physician and nurse staff on duty, the others have a physician and nurse on the part time basis. Most supervisors and selected employees have trained in first aid.

Since the outbreak of the Goodrich liver cancer, more companies have started providing SMA-12 or other tests to employees who are handling VCM. However, few of the companies indicated that they are conducting medical surveillance of their employees as a routine program.

Because Dow Chemical Company is the leading producer of chlorinated hydrocarbons in this country, they have put more emphasis on liver function testing of their employees. The medical surveillance program as presented to us by Dow (Table IV) can be used as a basis for the medical requirement in our proposed vinyl chloride standard.

## Engineering Control

Ventilation is still an effective method to control the VCM exposure. The control rooms in all the VCM and PVC plants are air conditioned, however, the air is withdrawn from the process area and discharged outdoors without any purification. Both the inlet and outlet air to the control room should be treated if a standard with very low or no permissible limit is proposed.

Engineering control methods are available for the control of VCM exposures, during sampling and loading operations. However, a reasonable time should be allowed for the implementation for such measures. This is also true for the installation of local exhaust ventilation systems. It may be more practical to allow time for the implementation of engineering control measures or an interim standard could be set to give employees some protection while the employer is provided with time for implementation of such controls. Usually, a time period of six months may be sufficient to install VCM emission control system and one year for ventilation systems.

## Personal Protective Equipment

All plants visited have self contained breathing apparatus (SCBA) or Gas Mask for emergency use and they indicated that every employee is trained to use such equipment. Two plants use canisters made for acid gases or ammonia other than organic vapor to equip their gas masks which is not considered to be suitable and one plant uses a quarter facepiece emergency escape respirator as a standard accessory for every employee and visitor in the process area containing hydrocarbons. This practice may give an employee a false sense of security and he may be exposed to high concentrations of VCM and still believe he is adequately protected.

Supplied air respirators, either in continuous flow or pressure demand made should be used for reactor cleaning or maintenance and repair work inside of a vessel containing VCM. One plant used supplied air for cleaning of reactors, however, no pressure reducer nor contaminant filtering device were found in the adjacent air supply. The present OSHA standard on breathing air quality is based on the recommendation of the Compressed Gas Association (CGA) which has higher tolerance for the common contaminants in the compressed air such as oil, carbon monoxide, etc. A low tolerance of these air contaminants and VCM in the breathing air and more specific, accurate and frequent monitoring methods should be proposed to insure that the quality of the breathing air is acceptable.

The use of gas masks equipped with activated charcoal adsorbent for the VCM will depend on whether we propose a standard with or without a permissible limit. Based on a test conducted by Gary Nelson of the Lawerence Livermore Laboratory, he indicated that the activated charcoal in a organic vapor canister or catridge is not a good VCM absorbent. From his results, the time to reach 1% breakthrough of VCM at a concentration of 1,000 ppm, 50% relative humidity, 22° C and a breathing rate of 53.3 Lpm is 3.8 minutes against 77 minutes for carbon tetrachloride. The present problem with organic vapor adsorbent is there is no indication of the life of such substance. The manufacturer's common practice is to set a shelf life of about three years from the date of manufacture with the assumption that the seal of the canister or catridge is remained intact. Once the seal is broken, the useful life will be one year.

Use of gas masks give an operator more freedom of movement than with a supplied air respirator or SCBA. This is particularly true for the process sample man and tank car loader. If gas masks are permitted to be used when a permissible limit of 5 or 10 ppm is proposed, the requirements for periodic renewal of canisters on different levels of VCM exposures should be specified in the proposed standard.

Safety glasses, goggles, hard hat and gloves are commonly used in all plants visited. Since liquid VCM is an irritant to skin and mucous membranes, the use of eye protective devices and gloves should be made mandatory for employees who may contact liquid VCM. The VCM vapor or gas is not considered to be absorbed through the skin at the present time, the use of ordinary protective clothing is useless and the need for an air supplied impervious suit is questionable in operations involving VCM exposure. The PVC reactor cleaning can be a dusty task and a cloth coverall or whole body covering is a good personal hygiene practice. If VCM is not found to be absorbed through the skin then the requirement for shower facilities may not be necessary.

## Housekeeping

Except for one plant, the general impression on housekeeping is that it is inadequate. This problem is more evident in the PVC plant since particulate material is involved. More effort is needed on immediate clean up spills and keeping the work environment in a cleaner, more orderly fashion.

Maintenance is another problem area. Preventive maintenance seems nonexistant and most of the plants have maintenance staff on day shift only. Since the leak of VCM from the process equipment, pipelines and fittings may be the significant source of unnecessary exposure in the industry, a more stringent maintenance program is imperative.

## Work Practice

Most of the plants visited have either written or informal procedures regarding operations where VCM exposure is likely such as process sampling, tank car loading, reactor cleaning and vessel entry. We may issue mandatory work practice procedures on these operations. A written procedure and checklist should be prepared for these operations and reactor cleaning and vessel entry should be performed by permit only and signed by the employer or his representative to insure that all precautionary measures regarding minimizing employee's exposure to VCM during such operations are enforced.

Quite a few chemicals are used in the manufacturing of VCM or PVC, some of them can be very toxic such as hydrogen chloride, chlorine or mercury salt and the toxic properties of some raw materials are not available at this time. It should be a safe practice to require the employer to evaluate the toxicity of every raw material he uses and establish written procedures for the safe handling of such substances.

## Training

Most employers indicate that they have training courses for VCM operators and regular safety meetings to educate their employees. Some companies use the word-by-mouth training techniques and such training are conducted by foreman. The success of such type of training is dependent on the quality of the instructor. In general, a written training manual should be preferred and should include items such as the hazards of VCM and other toxic raw materials, work practices, use and care of personal protective equipment, first aid, emergency procedures, fire fighting and safe handling of the VCM. It is imperative that an untrained employee should not be permitted to work in the VCM or PVC process area and refresher courses on these subjects should be given on a periodic basis. A monitoring system should also be established to insure that an employee is benefiting from such training.

## Waste Disposal

Both of the PVC plants claimed that the unreacted VCM is recycled back to the process. The off specification VCM is reprocessed to meet the requirement. One PVC producer discharges the scraps from reactor cleaning into a pond and another collects the waste into boxes for sale to a scrap dealer. One plant loads the PVC in box cars under pneumatic force. It is a closed system, any powder released from loading is sert back to the storage silos.

Since the toxic effect of PVC is not known to date, it may seem unreasonable to require the manufacturers to dispose of the PVC waste in impermeable bags since the bags probably made from PVC or to require the incineration of PVC or VCM as a means of disposal because the decomposition product is toxic. We may require procedures to be established for the destruction of these substances by a safe chemical method or just leave this paragraph open until we get more information.

## Conclusion

The exposure to VCM is less of a problem to the VCM producers than to the PVC producers because all the process equipment of the former are located outdoors with fewer employees and control is less expensive to implement. Most of the PVC manufacturing facilities are enclosed and more employees are involved in the production. Engineering Control is more expensive because of the high volume of air to be ventilated. However, control technology is readily available and the cost of compliance may not be prohibitive.

Lack of maintenance programs, monitoring activities, inadquate employee training, medical examination and surveillance, and poor housekeeping are the common observations found during this survey. We may put emphasis on these areas on our proposed standard on the VCM.

All manufacturers were very cooperative during this survey. They answered all questions we asked and gave us the information we needed. From this survey, we were given the chance to communicate with the production people, to find out which areas present potential exposures to VCM, what the producer has accomplished to control the exposures at each area, and at which areas further control of the problem and what enforcement is required. We sincerely believe that this type survey should be included in our regular rule-making procedures so far as health standards development is concerned.

## LIST OF FIGURES

1. Manufacturing of VCM by Direct Chlorination and Oxychlorination of Ethylene

2. Manufacturing of VCM by Direct Chlorination of Acetylene

3. Manufacturing of PVC by Suspension or Emulsion Polymerization

4. Manufacturing of PVC by Bulk Polymerization

## LIST OF TABLES

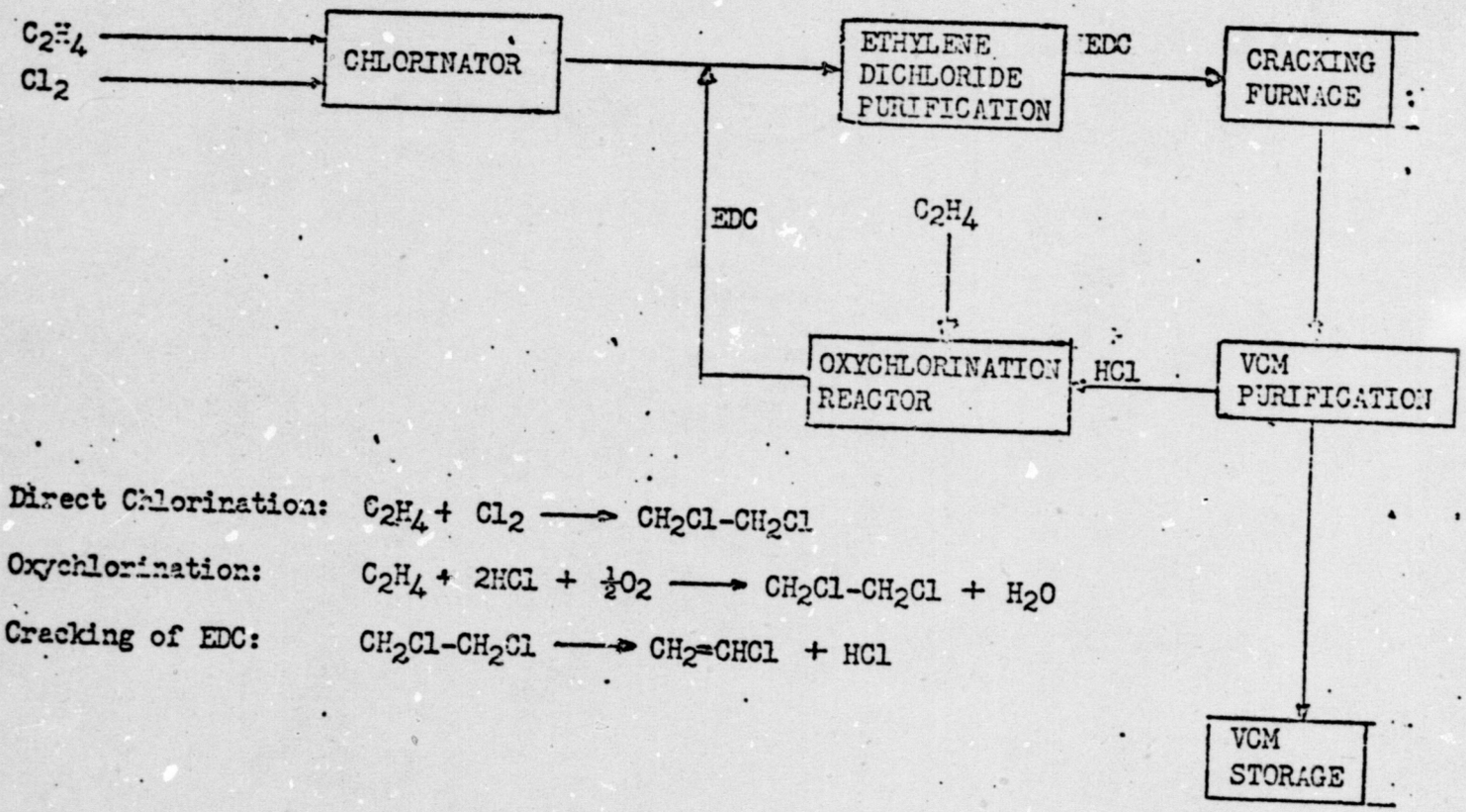
I. Manufacturing Facilities of Vinyl Chloride and Polyvinyl Chloride

II. Initial Monitoring Data From Plant A

III. VCM Monitoring Data From Plant B

IV. Medical Surveillance Program at Dow Chemical U.S.A.

FIGURE 1.. MANUFACTURING OF VCM BY DIRECT CHLORINATION AND OXYCHLORINATION

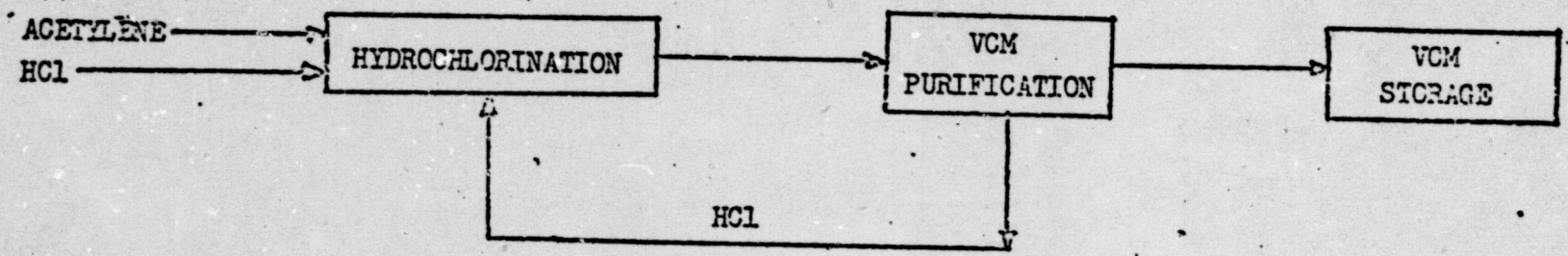



Direct Chlorination: $C_2H_4 + Cl_2 \longrightarrow CH_2Cl\text{-}CH_2Cl$

Oxychlorination: $C_2H_4 + 2HCl + \frac{1}{2}O_2 \longrightarrow CH_2Cl\text{-}CH_2Cl + H_2O$

Cracking of EDC: $CH_2Cl\text{-}CH_2Cl \longrightarrow CH_2{=}CHCl + HCl$

FIGURE 2. MANUFACTURING OF VCM BY DIRECT CHLORINATION OF ACETYLENE




$$CH{\equiv}CH + HCl \longrightarrow CH_2{=}CHCl$$

FIGURE 3. MANUFACTURING OF PVC BY SUSPENSION /OR EMULSION POLYMERIZATION

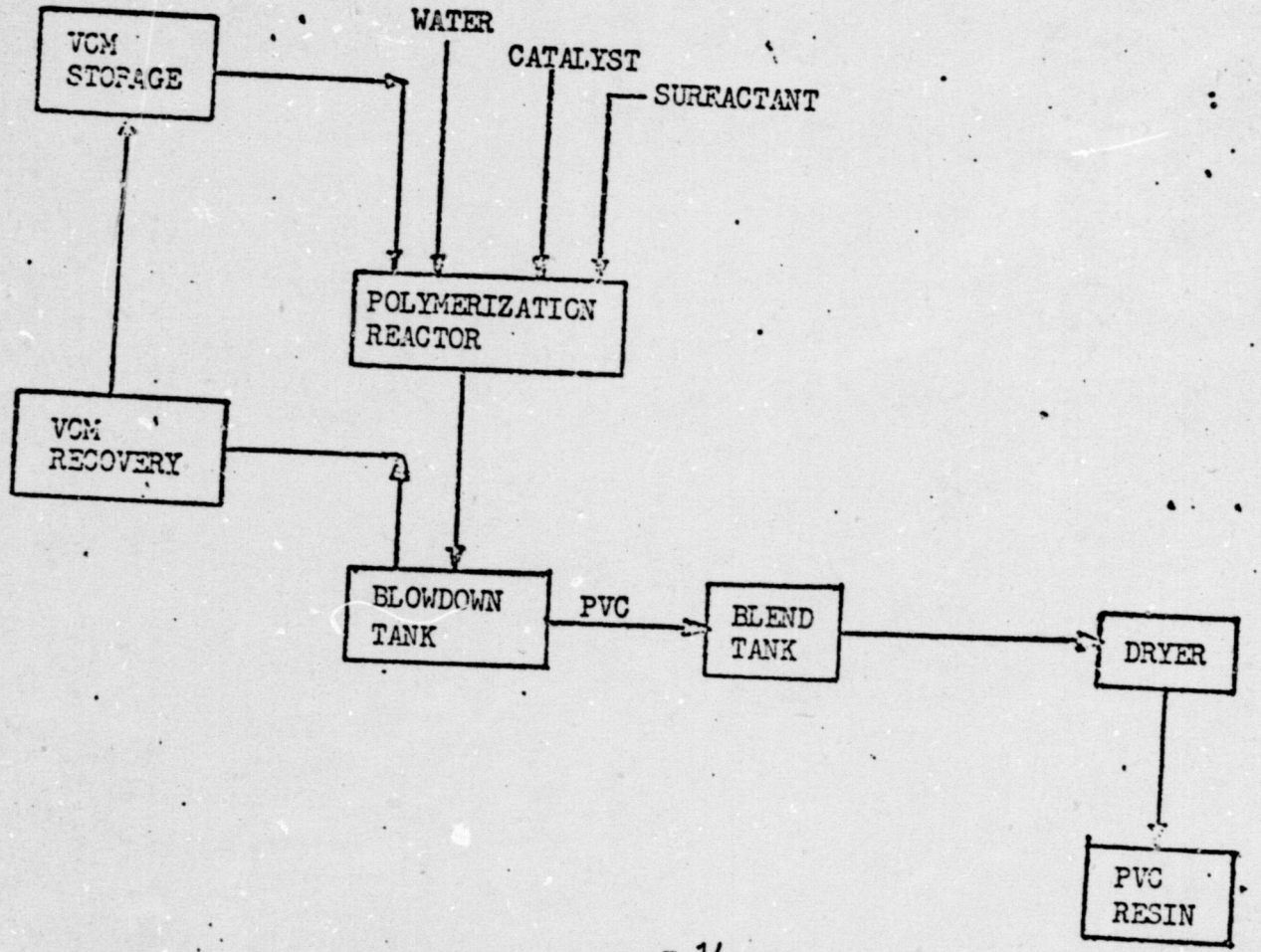


FIGURE 4. MANUFACTURING OF PVC BY BULK POLIMERIZATION

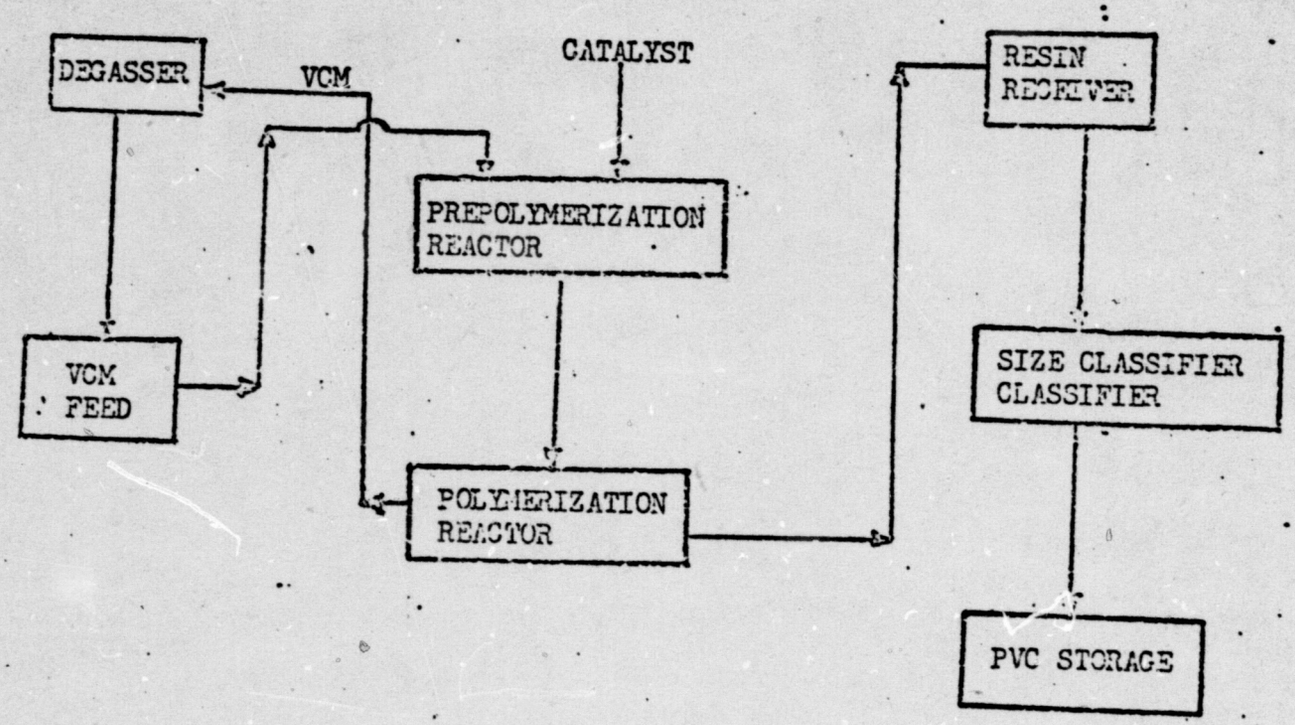


TABLE 1

MANUFACTURING FACILITIES OF VINYL CHLORIDE
and
POLYVINYL CHLORIDE

| Plant | Location | Process |
|---|---|---|
| Ethyl Corp. | Baton Rogue, LA | VCM- Direct and oxychlorination of ethylene |
| | | PVC- Suspension and emulsion polymerization |
| Shell Chemical Co. | Norco, LA | VCM- Direct and oxychlorination of ethylene |
| Dow Chemical Co. U.S.A. | Plaquemine, LA | VCM- Direct chlorination of ethylene |
| Allied Chemical Co. | Baton Rogue, LA | VCM- Direct and oxychlorination of ethylene |
| Goodyear Chemical Co. | Plaquemine, LA | PVC- Bulk polymerization |
| Monochem Corp. (Borden and Uniroyal) | Geismar, LA | VCM- Direct chlorination of acetylene |

INITIAL VCM MONITORING

DATA FROM PLANT A

Sampling Periods: November 1973

| Job Classification | Sampling Time hr. | VCM Concentration ppm |
|---|---|---|
| VCM Operator | 7.5 | 1.3 |
| VCM Operator | 7.5 | 1.7 |
| EDC Operator | 7.5 | 0.8 |
| EDC Operator | 25 min. | 0.5 |
| OXY Operator | 7.5 | 0.3 |
| VCM Loader | 3.0 | 8.7 |
| VCM Loader | 25 min. | 16.0 |
| VCM Loader | 3.5 | 13.4 |
| VCM Loader | 45 min. | 43.0 |
| Lab Technician | 10 min. | 3.2 |

## VCM MONITORING DATA FROM PLANT B

Sampling period: September 1972, March & April 1973
VCM Concentration: ppm (V/V)

| Job classification | Samples range high | Samples range low | Number of samples taken | TWA |
|---|---|---|---|---|
| Shift supervisor | 3.7 | 0.1 | 10 | 0.4 |
| VCM boardman | 3.6 | 0.03 | 18 | 0.6 |
| EDC boardman | 5.5 | 0.07 | 10 | 2.4 |
| Sample man | 13.0 | 0.1 | 12 | 0.7 |
| VCM loader | 158.0 | 0.05 | 30 | 4.2 |
| VCM loader | 13.5 | 0.05 | 30 | 2.9 |
| Shift supervisor | 13.0 | 0.03 | 20 | 0.4 |
| Junior operator | 13.5 | 0.03 | 32 | 2.3 |
| Q.C. specialist | 32.1 | 0.05 | 28 | 3.0 |
| Lab technician | 158.1 | 0.06 | 26 | 10.3 |
| Lab technician | 229.0 | 0.1 | 30 | 15.0 |
| Material controller | 0.3 | 0.05 | 10 | 0.1 |
| Instrument technician | 13.0 | 0.03 | 30 | 1.9 |
| Pipefitter | 13.0 | 0.03 | 10 | 4.5 |
| Millwright | 13.0 | 0.03 | 10 | 4.4 |
| Electrian | 13.0 | 0.03 | 10 | 3.5 |
| Laborer | 13.0 | 0.03 | 12 | 4.5 |

MEDICAL SURVEILLANCE

All contractor and Dow employees working in areas where chemicals may have toxic effect on liver have been included in plant medical surveillance program for several years. Originally tests obtained to determine liver toxicity were S.G.O.T., Thymol Turbidity, Cephalin Flocculation, and Bilirubin. We began obtaining SMA-12 in 1969. Approximately 300 to 350 employees are tested yearly. Several thousand persons have been tested over the years. We have never found any indication of liver toxicity due to chemical exposure. Plants included in this testing program are Glycol #1, Chlorinated Solvents, Vinyl, Chlorinated Methanes, Marine Tank Car Cleaning, Waste Disposal workers, and selected R & D personnel.

In 1971 we began a more comprehensive testing program on all employees engaged in operations. Medical history is taken as well as smoking history, any indication of weight loss or gain during past year is recorded - hemoglobin and urinalysis is done. Urinalysis includes blood, glucose, ketone, P.H., specific gravity, bilirubin and urobilinogen.

Additional procedures on those employees working in Vinyl Chloride area have been proposed, including EPA of chest, x-ray of hands, microscopic urinalysis, S.G.P.T., CBC, platelet count, forced expiratory volume and Fev,. Physical examinations have been recommended and we are now in the process of securing these procedures.

In event of single exposures breath sample for analysis is secured, physical examination by physician, SMA and other tests as indicated are secured.

Betty Doughty, R.N.
Medical Supervisor

ad

FEB 1974 E 1(d) 51

NIOSH Recommended Precautionary Monitoring and Control Procedures for Polymerization Processes Involving Vinyl Chloride

I. General Housekeeping Procedures

A. The spillage of Vinyl Chloride and Polyvinyl Chloride in and around the production facilities should be controlled as follows:

1. Housekeeping procedures should be implemented to assure immediate removal of VC and PVC material around polymerization operations including drying, packaging and loading operations.

2. Recovered PVC material which is to be packaged should be stored in closed containers.

3. Waste PVC material should be stored in closed containers and consideration should be given to the adequacy of its disposal and/or destruction. Care should be taken in the storage of closed containers to insure that unsafe conditions do not result from an internal build-up of pressure in the container.

B. Inventories of beginning and recovered quantities of VC and quantities of PVC produced, packaged and recovered should be made to determine losses and probable areas affected.

C. PVC material should be removed from overhead structures and conduits where it tends to collect.

D. Consumption of food should be permitted only in separate facilities provided for this purpose, and no food products should be permitted elsewhere in the polymerization facility.

II. Protective Clothing

A. A daily change of protective clothing including full coveralls, or the equilvalent, should be provided each employee in areas where possible exposure to VC PVC could occur. Clothing contaminated by accidental spills should be changed as soon as feasible.

B. Protective gloves and footwear, or footcovers, should be worn as appropriate in those PVC operations where exposure to PVC material is possible.

C. Protective head covers should be worn during PVC operations as appropriate (e.g. hard hats in those areas where physical protection of the head is necessary and hair coverings, or the equilvalent, in

operations such as cleaning of polymerization reactor tanks and packaging operations).

D. Where employees are engaged in maintenance or cleaning operations of polymerization reactors tanks they should wear full impervious suits to guard against skin contact of PVC material and VC vapors. Procedures for safe entry to confined spaces should be observed.

III. Showers

Showers at the termination of an eight-hour work shift should be mandatory for all workers with possible contact with VC-PVC.

IV. Monitoring

A. Environmental Monitoring

1. In-plant environmental monitoring programs should be implemented; and where workers are required to enter polymerization tanks, a survey of the VC concentrations should be made in the reactors immediately after opening, immediately prior to entry of maintenance personnel and during the tank cleaning operation.

2. Data obtained from the environmental monitoring program should be used to indicate those areas where efforts should be directed to reduce airborne levels of VC.

3. Positive programs to initially control VC levels well below the present Federal Standard of 500 ppm should be developed (some companies are targeting at 50 ppm) and efforts to further reduce levels should be given consideration concomitantly with the necessary modifications in engineering and design controls.

4. The concentration of VC in exhaust ventilation should be determined to estimate the amount of VC lost during operations and the possible exposure of personnel immediately outside the facility.

5. Monitoring for PVC particulate material should be accomplished to estimate the degree of exposure to this substance throughout the facility.

B. Personal Monitoring

1. Integrated, eight-hour personal monitoring samples should be obtained from those employees considered to receive the greatest exposure to VC or PVC.

2. Breathing zone samples should be obtained to complement environmental monitoring program for VC, and similar samples should be obtained for PVC.

V. Respiratory Protection

Because VC is a gas under ambient conditions and PVC is a solid under these conditions, it is recommended that respiratory protection for employees take these circumstances into consideration.

A. Where employees are engaged in cleaning and maintenance operations inside polymerization reactors they should be equipped with an atmosphere-supplied respirator in order to protect against both VC vapor and PVC particulates.

B. During housekeeping procedures and packaging operations where the possibility of PVC dust inhalation is a factor, it is recommended that an air-purifying respirator equipped with a mechanical filter designed to remove particulate material be worn. Respiratory protective devices which meet this requirement, as well as protect against VC vapors in concentrations less than 0.1% have been approved by the NIOSH Testing and Certification Laboratory and bear the numbers: TC-23C-40, TC-23C-47, TC-23C-48.

C. Where employees are engaged in transfer operations of VC from railway tankcars to storage facilities or at any similar transfer point which requires manual operations, they should wear a self-contained breathing apparatus (SCBA) during such operations to guard against unexpected release of VC during such operations.

D. Other operations involving possible exposure to VC or PVC should be evaluated as the individual situation exists and respiratory protection provided as appropriate.

Assistant Secretary of Labor
Occupational Safety and Health Administration
Department of Labor

DATE: MAR 11 1974

74(f)

Director, National Institute for
Occupational Safety and Health

Recommended Occupational Health Standard for the Manufacture of Synthetic Polymer from Vinyl Chloride

On January 22, 1974, representatives from the B. F. Goodrich Chemical Company informed NIOSH that the deaths of several employees of their Louisville, Kentucky, plant might have been related to occupational exposures. An immediate industrial hygiene walk-through survey of the facility was conducted by NIOSH and resulted in developing and transmitting to affected companies recommendations for precautionary monitoring and control procedures for polymerization processes involving vinyl chloride. On February 1, 1974, NIOSH/CDC conducted a briefing for other Federal agencies with health research responsibilities at which it was disclosed that four employees of the plant in question had died of angiosarcoma of the liver. Because of the extremely low incidence of this disease, estimated to be on the order of 20 to 30 deaths per year in the United States, the history of four cases in a five-year period in one plant was considered of great importance. It was concluded at the briefing that a new occupational cancer had been discovered: angiosarcoma of the liver. It was further concluded that this disease was associated with the manufacture of polyvinyl chloride and that vinyl chloride was the prime etiological candidate in producing the disease.

NIOSH, with the assistance of expert consultants from both industry and organized labor, began development of a recommended occupational health standard. These and other activities were discussed in more detail at the OSHA Informal Fact-Finding Hearing on Possible Hazards of Vinyl Chloride Manufacture and Use on February 15, 1974. It was also during this Hearing that Professor Cesare Maltoni of Bologna, Italy, presented the preliminary results of his research which showed induction of angiosarcoma of the liver and other organs, as well as the production of other cancers in rats exposed to vinyl chloride. The results of these studies identify vinyl chloride as a carcinogen and further confirm its role in inducing the cancers observed in the B. F. Goodrich workers.

Since the OSHA Hearing, NIOSH has learned of at least five additional cases of angiosarcoma of the liver. Two of these cases were diagnosed in the current working population at the same Louisville facility, while the other three involved deceased workers, one each from the Louisville facility, Union Carbide's South Charlestown plant, and Goodyear's Niagara plant.

Although vinyl chloride must be considered as a carcinogenic agent, the immediate problem appeared to be concentrated in polymerization facilities. Consequently, the attached NIOSH recommended standard only applies to such operations. This is not to say, however, that appropriate standards should not be developed for other exposures to the basic chemical. NIOSH is implementing further evaluation of the data, coupled with field observations, to determine exposure potentials in pre- and post-polymerization operations. You will be informed as further data and plans are developed.

As previously indicated, NIOSH considers this to be a most serious problem and strongly urges that expedited rulemaking be implemented by OSHA to insure that the health of exposed workers is promptly and adequately safeguarded.

We feel that, except where employers experience problems in obtaining air supplied respirators or environmental monitoring equipment, the attached recommendations can be implemented as soon as a standard is promulgated. The medical surveillance requirements which will be supplied in one to two weeks could also be implemented immediately with the possibility that some employers would need a short period of time for their medical staff or consultants to make arrangements for any special laboratory tests.

You should be aware that the consultants from industry who worked with us proposed that the recommended standard contain the concept of an allowable "working level" for vinyl chloride gas in the atmosphere, which they identified as a time weighted average of 50 ppm. They recommended that where workers were exposed to concentrations in excess of this level they should wear air-supplied respirators.

This concept of an allowable "working level" might seem justifiable in that Professor Maltoni found no liver tumors at 50 ppm, but there is the possibility that tumors might have been produced if a larger number of animals had been exposed at that concentration. Based on theoretical considerations, there is probably no threshold for carcinogenesis although it is possible that with very low concentrations, the latency period might be extended beyond the life expectancy. In view of these considerations and our inability to describe a safe exposure level as required in section 20(a)(3) of the Occupational Safety and Health Act, we rejected the concept of a threshold limit for vinyl chloride gas in the atmosphere.

Consequently, our recommendations as contained in the attached document are such that where any employee is exposed to measurable concentrations of vinyl chloride, as determined by the recommended sampling and analytical method, he shall wear an air supplied respirator. This recommendation is based on some preliminary information that the standard chemical cartridge respirators are inefficient in protecting against vinyl chloride. NIOSH is implementing a study to evaluate the degree of protection afforded by different types of respirators using vinyl chloride as the test gas. As information becomes available, it will be forwarded to OSHA as recommendations for alternative respirator usage. The employer is also required to develop a Control Plan to reduce airborne concentrations of vinyl chloride to levels not detectable by the recommended method.

As you will note in reviewing the recommended standard, there are references to the "sampling and analytical method recommended by the Director." This method, in the form of a compliance sampling data sheet, will be forwarded to OSHA within a week. We now estimate that the level of sensitivity of our recommended method will be around one part per million, specifically for vinyl chloride.

The Office of Research and Standards Development, which is directed by Mr. Vernon D. Rose, has had lead responsibility in developing this recommended standard. As your professional staff review and evaluate our document, questions or requests for additional information should be directed to Mr. Rose.

Marcus M. Key, M.D.
Assistant Surgeon General

Attachment

# RECOMMENDED OCCUPATIONAL HEALTH STANDARD

FOR

# THE MANUFACTURE OF SYNTHETIC POLYMER FROM

# VINYL CHLORIDE

MARCH 11, 1974

U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health

## 1. SCOPE AND APPLICATION

This standard regulates the manufacture of synthetic polymer from vinyl chloride (chloroethene, Chemical Abstracts Registry No. 75014), in order to protect the health and safety of workers.

Vinyl chloride also known as vinyl chloride monomer (VCM), chloroethylene and chloroethene, is a colorless sweet smelling gas at ordinary temperature and pressure and has a boiling and melting point at one atmosphere of -13.8°C, and -153.71°C, respectively. Its chemical formula is $CH_2CHCl$ and it has a molecular weight of 62.50. Although noncorrosive at normal atmospheric temperatures, in contact with water and at elevated temperatures it accelerates the corrosion of iron and steel. Of considerable concern is the fact that vinyl chloride is easily ignited and has a lower and upper explosive limit of 3.6% and 26.4%, respectively.

## 2. DEFINITIONS

For the purpose of this standard:

a. "Assistant Secretary" means the Assistant Secretary for Occupational Safety and Health, U.S. Department of Labor or any person directed by him.

b. "Director" means the Director, National Institute for Occupational Safety and Health, or any person directed by him or the Secretary of Health, Education, and Welfare to act for the Director.

c. "Authorized employee" means an employee whose duties require him to be in the regulated area and who has been specifically assigned by the employer.

d. "Detectable levels" means the determination that airborne concentrations of vinyl chloride are in excess of the limit of sensitivity of the sampling and analytical method recommended by the Director.

e. "Clean change room" means a room where employees put on clean clothing; clean change room shall be contiguous to and have an entry from a shower room, when the shower room facilities are otherwise required in this standard.

f. "Closed container" is any container which is used to prevent the physical contact of employees with material containing vinyl chloride monomer.

g. "Closed system" means an operation involving vinyl chloride where containment prevents the release of vinyl chloride into regulated areas, nonregulated areas, or the external environment.

h. "Contaminated" refers to detectable levels of vinyl chloride monomer.

i. "Decontamination" means the inactivation of vinyl chloride to less than detectable levels or its safe disposal.

j. "Disposal" means the safe removal of vinyl chloride from the work environment.

k. "Emergency" means an unforeseen circumstance or set of circumstances, such as a ruptured transfer line, resulting in the release of vinyl chloride sufficient to produce acute symptoms among workers exposed or having contact with the vinyl chloride.

l. "External environment" means any environment external to regulated and nonregulated areas.

m. "Regulated area" means an area where entry to and exit from a vinyl chloride workplace is restricted and controlled.

n. "Nonregulated area" means any area under the control of the employer where entry and exit is neither restricted nor controlled.

o. "Protective clothing" means clothing designed to protect an employee against contact with or exposure to vinyl chloride.

p. "Waste resin" means any resin or other vinyl chloride reaction product which has been removed from vessels during clean-up operations, or which has been collected as a result of in-plant housekeeping operations.

3. REQUIREMENTS FOR REGULATED AREAS

A regulated area shall be established where synthetic resins containing vinyl chloride are manufactured. These regulated areas shall include but are not limited to vinyl chloride loading or unloading operations, storage, and transfer facilities; synthetic resin polymerization processes and operations; and resin handling, compounding, packaging and storage areas. Access shall be restricted to authorized employees only. All such regulated areas shall be controlled in accordance with the following requirements.

a. Routine Operations

(i) Initial concentration of vinyl chloride in all regulated areas shall be determined by performing air measurements at strategic sampling points under normal operating conditions. These initial sampling points must be selected by a professional industrial hygienist and will serve as monitoring locations for future environmental measurements.

The sampling pattern shall be adequate to represent the environment of the controlled area.

(ii) Where detectable levels of vinyl chloride are measured, a Control Plan to reduce such levels shall be developed and implemented. The Plan shall consist not only of establishing goals for reducing vinyl chloride levels by designing and introducing engineering and process controls, but shall also identify plans for developing additional (healthful) work practices. Target dates shall be established for all goals and the Plan must be updated at least on an annual basis. Copies of the Control Plan shall be posted in all regulated areas and be provided to all authorized employees.

(iii) There shall be periodic tests for process or equipment leaks and for emission of vinyl chloride which may result from work practices. The frequency of these tests shall be such as to insure the integrity of equipment, adherence to proper work practices, and to determine achievement of the goals of the Control Plan. Tests shall be performed at each sampling point at least daily or more frequently if concentrations of vinyl chloride are in excess of those established in the Plan. When such levels are exceeded, additional samples to identify sources of contamination shall be taken. Results of all such tests shall be made available to authorized employees in such a manner as to evaluate achievement of goals contained in the Control Plan.

(iv) Until exposures to vinyl chloride are reduced below detectable levels, employees entering any regulated area shall be provided with and required to wear and use a full-face, supplied air respirator, of the continuous flow or pressure demand type in accordance with §1910.134.

(v) In operations involving loading or unloading vinyl chloride monomer from tank cars, trucks, barges, or other conveyance equipment, each transfer line and each vapor-equalizing line shall be equipped with vent connections permitting, at the completion of the transfer, pressure to be vented and the hose purged with an inert gas in such a manner to preclude any employee exposure. Specific and detailed transfer procedures shall be developed and provided to involved employees in written form.

(vi) Employees shall be provided with and required to wear, clean, full-body protective clothing (smocks, coveralls, or long-sleeved shirt and pants), and gloves prior to entering the regulated area.

(vii) Prior to each exit from a regulated area, employees shall be required to remove and leave protective clothing and equipment at the point of exit and at the last exit of the day, to place used clothing and

equipment in impervious containers at the point of exit for purposes of decontamination or disposal. The contents of such impervious containers shall be identified as required under paragraph e(2)(i) of this standard.

b. Reactor and Vessel Entry

(i) A reactor and vessel entry procedure shall be developed and provided to involved employees in written form. Employees shall be familiarized with the procedure and shall be trained and rehearsed in the techniques provided for in the procedure. Emphasis shall not only be placed on concern for potential exposure to vinyl chloride but shall also include appropriate precautions for entry into confined spaces.

(ii) Techniques shall be developed and applied to minimize to the maximal practicable extent employee exposure to vinyl chloride when opening any closed vessel. Examples of effective methods are the application of heat or suction to the vessel prior to opening, or use of sufficient exhaust ventilation around the vessel. Where operations such as cleaning or maintenance conducted inside an open vessel could result in the liberation of vinyl chloride, suitable procedures such as exhaust ventilation shall be developed and implemented to insure that vinyl chloride is not released into the general work environment.

(iii) Exhaust air shall not be discharged to regulated areas, nonregulated areas, or the external environment unless decontaminated.

(iv) All piping to and from the vessel shall be blanked or otherwise isolated prior to entry.

(v) Employees entering the reactor or vessel shall be provided with and required to wear and use a full-face, supplied air respirator, of the continuous flow or pressure demand type in accordance with §1910.134.

(vi) Employees entering the reactor or vessel where levels of vinyl chloride are monitored and are found to not exceed ambient levels external to the vessel shall be provided with and required to wear clean, full body protective clothing (coveralls or long-sleeved shirt and pants), gloves, footwear or foot coverings, and head covering. Where vessel levels are in excess of ambient levels, employees shall instead be provided with and required to wear impervious clothing to prevent skin contact of vinyl chloride or other materials containing vinyl chloride.

(vii) After each exit from the reactor or vessel, employees shall be required to remove and leave protective clothing and equipment at a designated point in the regulated area, and at the end of each work shift to place used clothing and equipment in impervious but vented containers for the purpose of decontamination or disposal. The contents of such impervious containers shall be identified as required under paragraph e(2)(i) of this standard.

(viii) Employees engaged in reactor cleaning or other operations involving vessel entry shall shower at the end of the work shift.

c. Maintenance and Decontamination Activities

(i) Emphasis shall be placed upon immediate clean up of spills, periodic inspection, prompt repair of equipment and leaks, and proper handling, storage and disposal or decontamination of materials to prevent airborne contamination and accidental skin contact with vinyl chloride. Because vinyl chloride is a gas at normal temperatures, waste materials, equipment, and other sources of the monomer in closed containers, shall not be placed in areas of excessive temperature or sunlight since build-up of internal pressure may result in rupture of the container, fire or explosion.

(ii) Waste resins or other materials contaminated with vinyl chloride shall be placed in closed containers identified as required under paragraphs e(2)(i) or (ii) of this standard.

(iii) Appropriate procedures shall be developed and implemented for the decontamination and/or dispoal of all such waste material.

(iv) In clean-up of leaks or spills, maintenance or repair operations on contaminated systems or equipment, or any operation involving work where direct contact with vinyl chloride monomer could result, each authorized employee involved in such operations shall be provided with and required to wear clean, impervious garments, including gloves, boots and continuous air supplied hoods in accordance with §1910.134, be decontaminated before removing the protective garments and hood; and be required to shower upon removing the protective garments and hood.

d. General Regulated Area Requirements

1. Employee identification.

A daily roster of employees entering regulated areas shall be

established and maintained. The rosters or a summary of the roster shall be retained for a minimum period of 20 years by the employer or successors thereto. The rosters and/or summaries shall be provided upon request to authorized representatives of the Assistant Secretary and the Director. In the event that the employer ceases business without a successor, rosters shall be forwarded by registered mail to the Director.

2. Emergencies.

In an emergency, immediate measures including but not limited to the requirements of subdivisions (i), (ii), (iii), (iv), and (v) of this subparagraph shall be implemented.

(i) The potentially affected area shall be evacuated as soon as the existence of the emergency has been determined.

(ii) Hazardous conditions created by the emergency shall be eliminated and the potentially affected area shall be decontaminated prior to the resumption of normal operations.

(iii) Special medical surveillance by a physician shall be instituted within 24-hours for employees present in the potentially affected area at the time of the emergency. A report of the medical surveillance and any treatment shall be included in the incident report, in accordance with paragraph (g)(3) of this standard.

(iv) Where an employee has a known contact with liquid vinyl chloride such employee shall be required to shower as soon as possible, unless contraindicated by physical injuries.

(v) An incident report on the emergency shall be reported as provided in paragraph (g)(3) of this standard.

3. Hygiene facilities and practices.

(i) Storage or consumption of food, storage or use of containers of beverages, storage or application of cosmetics, smoking, storage of smoking materials, tobacco products or other products for chewing, or the chewing of such products, are prohibited in regulated areas.

(ii) Where employees wear protective clothing and equipment clean change rooms shall be provided, in accordance with §1910.141(e)(3).

(iii) Where employees are required by this standard to wash, washing facilities shall be provided in accordance with §1910.141(d) (1) and (2)(ii) through (vii).

(iv) Where employees are required by this standard to shower, shower facilities shall be provided in accordance with §1910.141(d)(3).

4. Contamination control.

(i) Regulated areas, except for outdoor systems, shall be maintained under negative pressure with respect to nonregulated areas. Local exhaust ventilation may be used to satisfy this requirement. Clean tempered makeup air shall replace air removed. Exhaust air shall not be discharged to regulated areas, nonregulated areas, or the external environment unless decontaminated.

(ii) Any equipment, material, or other item taken into or removed from a regulated area shall be done so in a manner that does not cause contamination in nonregulated areas or the external environment.

(iii) Decontamination procedures shall be established and implemented to remove vinyl chloride from the surfaces of materials, equipment and the decontamination facility.

e. Signs, Information, and Training

1. Signs.

(i) Entrances to regulated areas shall be posted with signs bearing the legend.

CANCER-SUSPECT AGENT AREA

AUTHORIZED PERSONNEL ONLY

(ii) Entrances to regulated areas containing operations covered in paragraph 3(c) of this standard shall be posted with signs bearing the legend:

CANCER-SUSPECT AGENT IN THIS AREA. IMPERVIOUS SUIT INCLUDING GLOVES, BOOTS, AND AIR-SUPPLIED HOOD REQUIRED AT ALL TIMES. AUTHORIZED PERSONNEL ONLY.

2. Container contents identification.

(i) Containers of waste or other materials contaminated with vinyl chloride shall be labelled as follows.

VINYL CHLORIDE CONTAMINATED MATERIAL

CANCER SUSPECT AGENT

DISPOSE OF OR DECONTAMINATE USING

APPROVED PROCEDURES

(ii) Containers of synthetic polymers made from vinyl chloride shall be labelled as follows.

SYNTHETIC VINYL CHLORIDE POLYMER

VINYL CHLORIDE IS A CANCER SUSPECT AGENT

POLYMER CONTAINS __*% BY WEIGHT UNREACTED

VINYL CHLORIDE

*(To be analytically determined by manufacturer and appropriate value entered on labels.)

(iii) Containers of vinyl chloride shall be labelled as follows.

VINYL CHLORIDE

DANGER! EXTREMELY FLAMMABLE LIQUID AND GAS UNDER PRESSURE

CANCER SUSPECT AGENT

HARMFUL IF INHALED

MAY POLYMERIZE VIOLENTLY UNDER FIRE CONDITIONS OR LOSS OR REMOVAL OF INHIBITOR

Keep away from heat, sparks, and open flame.
Keep container closed.
Use with adequate ventilation.
Avoid breathing vapor.
Avoid contact with skin.
Keep cylinder out of sun and away from heat.
Container should be grounded when being emptied.
Never drop cylinder.

FIRST AID: If inhaled, remove to fresh air. If not breathing give artificial respiration, preferably mouth-to-mouth. If breathing is difficult, give oxygen. Call a physician.

In case of:

Fire - Use water spray, dry chemical, or $CO_2$.

Spill or Leak - For small spills, evacuate area and permit to evaporate. For large spills or leaks, evacuate area. Dike or flush to ground and let evaporate. Do not flush to sewer because of explosion hazard.

3. Training and indoctrination.

(i) Each employee, prior to being authorized to enter a regulated area, shall receive a training and indoctrination program including, but not necessarily limited to:

(a) The nature of the carcinogenic hazards of vinyl chloride monomer, including local and systemic toxicity;

(b) The specific nature of the operation involving vinyl chloride monomer which could result in exposure;

(c) The purpose for and application of the medical surveillance program;

(d) The purpose for and application of decontamination practices and purposes;

(e) The purpose for and significance of emergency practices and procedures;

(f) The employee's specific role under normal operating or emergency conditions;

(g) Specific information to aid the employee in recognition and evaluation of conditions and situations which may result in the release of vinyl chloride monomer;

(h) The purpose for and application of specific first aid procedures and practices;

(i) A review of this standard at the employee's first training and indoctrination program and annually thereafter.

(ii) Specific emergency procedures shall be prescribed, and posted, and employees shall be familiarized with their terms, and rehearsed in their application.

(iii) All materials relating to the program shall be provided upon request to authorized representatives of the Assistant Secretary and the Director.

f. Environmental Monitoring and Recordkeeping

(i) Environmental concentrations of vinyl chloride shall be determined through the use of methods for sampling and analysis

recommended by the Director or by methods of at least equal sensitivity.

(ii) Employees or their representatives shall be provided with the opportunity to observe environmental monitoring activities and shall have access to the results.

(iii) Complete and accurate records of all environmental measurements shall be maintained for at least 20 years by the employer or successors thereto and shall be provided upon request to authorized representatives of the Assistant Secretary or the Director.

g. Reports

1. Operations.

Within 60 days the following information shall be reported in writing to the appropriate Occupational Safety and Health Administration (OSHA) Area Director. Any change in such information shall be similarily reported within 15 calendar days of such change.

(i) A brief description and in-plant location of the area(s) regulated and the address of each regulated area.

(ii) The number of employees in each regulated area, during normal operations, including maintenance activity.

(iii) A copy of the Control Plan as developed under paragraph 3(a)(ii).

(2) Environmental Measurements.

On a semi-annual basis the results of measurements taken at strategic sampling points, presented in such a manner as to identify achievement of goals established in the Control Plan, shall be reported in writing to the appropriate OSHA Area Director.

(3) Incidents.

Incidents which result in the release of vinyl chloride monomer into any area where employees may be potentially exposed shall be reported in accordance with this subparagraph.

(i) A report of the occurrence of the incident and the facts obtainable at that time including a report on any medical treatment of affected employees shall be made within 24 hours to the appropriate OSHA Area Director.

(ii) A written report shall be filed with the appropriate OSHA Area Director within 15 calendar days thereafter and shall include:

(a) A specification of the amount of material released, the amount of time involved, and an explanation of the procedure used in determining this figure;

(b) A description of the area involved, and the extent of known and possible employee exposure and area contamination;

(c) A report of any medical treatment of affected employees, and any medical surveillance program implemented; and

(d) An analysis of the circumstances of the incident, and measures taken or to be taken, with specific completion dates, to avoid further similar releases.

h. Medical Surveillance

(To be provided by NIOSH as soon as possible.)

7(L)

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# INTERAGENCY COLLABORATIVE GROUP ON ENVIRONMENTAL CARCINOGENESIS

## Vinyl Chloride Exposure and Neoplastic and Non-Neoplastic Disease

Office of the Scientific Coordinator
for Environmental Carcinogenesis
Division of Cancer Cause and Prevention
National Cancer Institute

AGENCIES CONTRIBUTING TO PROGRAM DISCUSSIONS
ON VINYL CHLORIDE EXPOSURE AND
CARCINOGENESIS



I. Department of Labor/Occupational Safety and Health Administration

II. National Institute of Occupational Safety and Health (NIOSH)

III. Center for Disease Control (CDC)

IV. Food and Drug Administration (Bureau of Foods) (FDA)

V. Food and Drug Administration (Bureau of Drugs)

VI. Consumer Product Safety Commission (CPSC)

VII. Environmental Protection Agency (EPA)

VIII. National Cancer Institute (NCI)

IX. Armed Forces Institute of Pathology (AFIP)

X. National Institutes of Health (NIH)

THE FOLLOWING IS AN UNEDITED TRANSCRIPT OF MATERIAL PRESENTED BY VARIOUS AGENCIES REPRESENTED AT THE NINTH MEETING OF THE INTERAGENCY COLLABORATIVE GROUP ON ENVIRONMENTAL CARCINOGENESIS.

The ninth meeting of the Interagency Collaborative Group on Environmental Carcinogenesis, held on April 17, 1974, at the National Library of Medicine, was devoted entirely to discussions of the vinyl chloride problem The Chairman gave a brief introduction, mentioned the previous meetings held by NIOSH and OSHA, and the task groups formed by various government agencies. He indicated that this is probably only the tip of the iceberg and that there may be other chemicals to which man is exposed, either at the work place or in the environment, which may present similar surprises in the future. He then called on Dr. Donald Lassiter from OSHA to present his report.

Occupational Safety and Health Administration

Dr. Lassiter brought the membership up to date on the actions taken by OSHA up to this time and what actions were on the horizon for the near future. Most have probably read and know about the emergency temporary standards promulgated by OSHA for vinyl chloride. The standard was principally based on the results of the fact finding hearing held on February 15. It was at this hearing that Dr. Cesare Maltoni presented his results up to that time, which demonstrated the induction of angiosarcoma of the liver in his rats exposed down to concentrations as low as 250 ppm. At that time, he had another group of rats (about 60 in number) exposed to 50 ppm and had observed no angiosarcomas in these animals. It was also significant that tumors other than angiosarcomas were found in these animals, including lung tumors and some other metastases. Based primarily on the results of that public hearing, the Assistant Secretary for Labor, Stender, decided to promulgate an Emergency Standard based on this preliminary knowledge to a level of 50 ppm. At the time prior to the promulgation of that Emergency Standard, the standard was 500 ppm of vinyl chloride as a ceiling value and it was, of course, readily recognized that this was presenting an extreme hazard to workers. With the mechanisms involved in the promulgation of standards, it was considered that this would be the most feasible way to remedy the situation quickly. In addition, after the hearing, NIOSH, which has the responsibility for research and standards development, sent to OSHA their recommendations for a standard for vinyl chloride. Basically, the NIOSH proposal was a series of work practices for the polymerization of vinyl chloride, which is where most of the known cases of angiosarcoma had occurred, and involved the institution of work practices, including the wearing of respiratory protective devices when vinyl chloride was detected. The detection was based upon a specified technique sensitive to approximately 1 ppm. This detection technique is undergoing some further investigation by NIOSH and perhaps will be specified in greater detail with the permanent standard. So, when OSHA promulgated the emergency standard, they had the NIOSH recommendations and, of course, the recommendations included only the polymerization of V.C. OSHA felt that it was necessary to also consider the synthesis of V.C. and the possibility of the downstream exposure to V.C. which was entrapped in resin. To date,

OSHA has good environmental exposure knowledge of vinyl chloride synthesis and polyvinyl chloride synthesis, that is the polymerization of V.C. The downstream use of the resins made from V.C. in terms of exposure is relatively unknown. OSHA has queried the companies, but they have not reported back, except in very fragmentary form, the results of their measurements downstream. As most probably are aware, V.C. resin is made to produce a number of synthetic plastic products and thousands of workers are involved on the downstream side. There are several processes that are used to make PVC from VC. Dependent upon the process, there may be more of the VC monomer entrapped in the more porous resins. It has been reported that some of the resins may contain at the packaging area as high as 800 ppm of VC entrapped in a very porous resin, to as low as 1 ppm in some less porous resins. So, as yet, the problem is undefined, but the standard that has been promulgated will, of course, cover all of these situations. Dr. Lassiter said he was going to present some data that EPA may have further comments on later. He had attended a meeting a couple of days ago in Chicago at the Industrial Biotest Laboratories. This group has been contracted by the Manufacturing Chemists Association to run some animal studies based primarily on Maltoni's findings. The Industrial Biotest Laboratories are running three species (rats, mice, and hamsters) at 50 ppm, 200 ppm, and 2,500 ppm of VC. The meeting was called the week of April 8 when it was discovered and reported to the sponsoring organization (MCA) that the laboratories were finding angiosarcomas of liver in mice at 50 ppm of VC. Basically, the protocol of the exposure was that 200 animals of each species, 100 of each sex, would be exposed to each level. So, for example, at 50 ppm there would be 200 rats, 200 mice, and 200 hamsters (100 of each sex) exposed. The tumors, the angiosarcomas, reported to date included one in a male mouse, one in a female mouse exposed at 50 ppm. At 200 ppm, there were four angiosarcomas of the liver reported, and at 2,500 ppm, seventeen angiosarcomas of the liver in mice (see Attachment I). The experiment has been ongoing for seven months now, it was initiated the 10th of September. The tumors began appearing after approximately six months, that is, the middle to latter part of March. There have been no tumors observed in the other animals, that is the rats or the hamsters, to date. The investigators conducting the study explained that they fully expected to see more tumors at the 50 ppm level in these animals. They base this on the fact that the experiment had been going for seven months and that the tumors observed were fairly recent. The protocol is a seven hour, five days a week, exposure. They do, of course, have people over the weekend working full time, but no exposure occurs during that time. The animals are Charles River mice. In view of what Dr. Richardson had drawn up in his handout, regarding the sensitivity of a couple of strains of mice to angiosarcomas, that is, the H.R. strain and the Swiss albinos having some normal incidence of angiosarcoma in the control populations, OSHA asked the investigators about this possible incidence in their control animals with the Charles River strain. They reported that having done this type of pathology on some 50 to 60 thousand mice during the past years, they have never observed angiosarcoma

of the liver in this strain of mouse. So, this is something to consider along with what we are seeing in some other strains.

There was a high incidence of mortality due to other causes in the mice. Out of 100 male mice exposed at 50 ppm, to date 31 of them have died. This includes the four that died from tumors. There were two other tumors reported in the male mice at 50 ppm. These two skin tumors metastasized to the lung, it was believed, the location was not specified. OSHA just received this information recently, and will evaluate it in concert with NIOSH. NIOSH probably made a good recommendation initially to OSHA. This actually means that workers, based on NIOSH recommendations, if implemented, would not be exposed. OSHA has a proposed permanent standard that should be published, probably in the Federal Register, based on the NIOSH recommendations which would, in effect, limit exposure down to the method specified for detection. Workers exposed, where there were detectable amounts, would, of course, be required to wear the respiratory protective devices and institute the other work practices.

Maltoni exposes animals with food in the cage and there is some speculation that there may have been a variable that needed to be controlled. In the Biotest study, the animals are being exposed without food; food being supplied after the exposure periods. So there is a high rate of cannibalism among the animals during the exposure periods. Since rodents are nocturnal eaters, the question was asked about the exposure time. Dr. Lassiter assumed that they are exposed during the day. The cage sizes, the exposure chambers, are 90.2 cubic meters and they hold 600 animals per chamber. These include 200 of each of the three species. The three species were apparently in the same chamber, as there were 600 animals per chamber.

As to the mortality at 50 ppm, to date 31 male and 9 female mice have died. This is at 7 months. At 5 months, the figure was 26 males and 6 females. Most of the deaths occurred during the first 90 days.

Dr. Lassiter maintained that this is basically where OSHA stands at this time. Mr. Stender has been out of the country for the past few days and has not been briefed on these latest developments.

Other deaths in mice were: at 200 ppm, there were 7 males, 13 females that died, and at 2,500 ppm, there were 18 males and 13 females. The 31 seems a little excessive, but they did not bother to explain that (i.e., Industrial Biotest). In the controls, they had 16 males and 5 females dead at 7 months. No tumors were reported in rats or hamsters. The mortality in rats stands at: 4 males, 4 females in controls; at 50 ppm, 10 males and 8 females; at 200 ppm, 6 males and 9 females; and at 2,500 ppm, 5 males and 7 females. The mortality in hamsters: in controls, 13 males and 22 females; at 50 ppm, 20 males and 20 females; at 200 ppm, 22 males and 29 females; and at 2,500 ppm, 27 males and 27 females. A question was raised about the proposed standard limiting

the exposure to the amounts detected. What does that mean? Dr. Lassiter explained that it is based on amounts detected by recommended sampling and analytical technique. This sensitivity is approximately 1 ppm. This is an interim recommendation made by NIOSH to OSHA; at this time, they are firming up a recommendation for the actual sampling technique for the permanent standard. The technique is being worked out and will be a gas sampling tube, either a tube per se or a charcoal tube with absorbent dilution and analyzed with gas chromatography or an equally sensitive method.

At this point, Dr. D'Aguanno asked about the probable occupational exposure levels to VC. He thought that one industrial study indicated exposure levels for 20 years of about 100 ppm. (Editor's note: Speculations have been made elsewhere and they are many orders of magnitude above this level, as indicated in comments later by Dr. J. Wagoner.)

The question is still open whether industry can get down to the 1 ppm level of sensitivity. At present, industry says this is impossible and it will be something that will have to be resolved. In the plants inspected by OSHA, there are some open air plants that present very low concentrations, but again where EPA is concerned, they are extremely hazardous. In the polymerization of VC, OSHA has not, and NIOSH probably has not either, seen any plant where they do not have some type of a problem. The lowest seen is around 10 ppm, or claims to operate in that range. In general, from what OSHA has seen, industry has more or less self-imposed a 50 ppm standard, which they claim they have been using for some time, but there are excursions above that level. OSHA has seen some levels in the past week, even in the newer plants, where they have a background of approximately 18 ppm, but they have some excursions up to over 100 ppm. So, it does fluctuate quite a bit. With the polymerization process, they open the vats to clean them out and there are fluctuations that can be very low at one time and the next minute can be very high. It has been reported to OSHA, that is in an open air facility, that about half of the workers were receiving less than one part per million.

Dr. Kraybill thanked Dr. Lassiter for his excellent report and asked the next speakers, Dr. Joseph Wagoner from NIOSH (Cincinnati) and Dr. Clark Heath from CDC (Atlanta), to make their presentations.

National Institute of Occupational Safety and Health

Being a firm believer of the adage that a picture is worth 10,000 words, Dr. Wagoner presented a number of slides on the status of VC investigators at NIOSH, including slides on the physical characteristics of VC, the two main types of processes, the number of plants with PVC operations, the estimated number of production workers in these facilities in the U.S. and in the world to date, and some of the uses of VC and the resins. He

also at the Union Carbide plant where the estimate is that 50,000 people have worked there. NIOSH does not know what portion of them have been exposed to VC or the co-polymers. It is probably premature to say anything about what NIOSH's findings are other than that by just looking at the proportionate distribution of the death certificates, we are seeing what seems to be very consistent with what Dr. Selikoff is reporting and what the Harvard group has reported, in that there is an unusual frequency of liver cancer and a very high frequency of lung cancer and brain malignancies. Essentially, that is where NIOSH investigations are in the PVC production facilities. NIOSH is working very closely with CDC people who are attempting to confirm the pathology on each case that NIOSH has and prepare data sets from which NIOSH will implement more intense medical screening than was recommended to the Department of Labor, which specifically would include sputum cytology examination because of Dr. Maltoni's observations at the OSHA hearings. NIOSH had direct correspondence with Clairol in June of last year, because NIOSH has been undertaking for about 1½ years, a general study of cosmotologists in the Western U.S. The indication was at that point in time they became very concerned. The month of March, which seems to be a very critical time in this whole unknown that we are talking about, was the date that the companies notified the aerosol companies that they would no longer provide them with VC. NIOSH has documentation of that. They have seen letters from one or two of the manufacturers of VC where they said essentially they will no longer provide it. March was the date that the MCA initiated their discussions and negotiations with Tabershaw and Associates for a long-term cohort effects study of chronic disease, and March was also the date that the MCA initiated their efforts with the Biotest group. What anyone knew last March as to what was coming on the scene in the U.S., one can only speculate; however, we can say that the Federal government does not know at this time.

NIOSH, since making recommendations to its own organization and transmitting them to Labor, has cancelled every visit into every facility in the U.S., pending the acquisition of respirators. They have also developed a routine policy matter that no one goes into any of the facilities where carcinogens are involved without the benefit of protective clothing and adequate respiratory protection. Noteworthy is the fact that when NIOSH indicated to one of the facilities that they wanted to go in to evaluate their situation but did not have the respirators and asked the management to provide them with respirators, they were denied the benefit of them and the visit was cancelled. The reason was that NIOSH was going to shake the workers up.

A copy of Dr. Wagoner's summary is attached (Attachment II). Dr. Wagoner indicated that to the best of his knowledge, Dr. Maltoni will be presenting his findings at the May 10 meeting at the NYAS. With regard to the results that were released in Chicago the other day from the MCA-sponsored study, 31 of the animals, in fact, were deceased, with two angiosarcomas. The available pathology on these animals is unknown. Dr. Wagoner stated that he

believed that there was a tremendous amount of carnibalism involved in the animals. Dr. Lassiter stated that this was also his impression, but a number of these that have died were not available for assay. Dr. Kraybill then alluded to the summary report on angiosarcomas by Dr. Howard Richardson, EPA, and indicated that this report suggests areas for further epidemiological, and perhaps experimental, studies.

Dr. Kraybill next introduced Dr. Clark Heath, Center for Disease Control. His statement follows:

Center for Disease Control

To Dr. Heath's knowledge, the first indication that NIOSH had of the liver angiosarcoma cases was in the middle or latter part of January. On January 24, they arranged a site visit to the Louisville plant to look over the situation, and asked CDC to provide a medical epidemiologist to join them. A member of the CDC Epidemiology Intelligence Service, Dr. Henry Falk, met with NIOSH and OSHA representatives and visited the B.F. Goodrich plant at Louisville, Kentucky, where they received their first-hand experience with this problem. In the ten days following, Dr. Falk returned to Louisville and, working closely with the plant physician, obtained information, medical records, and pathology specimens on all of the then known cases of liver tumors, which included two cases of angiosarcoma. He collected specimens, in addition, from another case of liver tumor, at that time called hepatoma, and also obtained materials and clinical information of four cases of non-malignant hepatic disease, which Drs. Johnson and Creech had obtained by going through their medical records.

So, at that time, within the first two weeks after CDC learned of the situation, they knew of three cases of angiosarcoma, and one of another liver tumor, at that time called hepatoma, and the non-malignant liver cases. These were taken to NIH and presented to Dr. Louis Thomas and Dr. Hans Popper. The first thing that happened was that the case of hepatoma became a case of angiosarcoma, so that there now were 4 cases of angiosarcoma. That, in itself, is pretty remarkable at that stage because hepatoma is a rather common liver tumor, whereas angiosarcoma is very rare. Dr. Heath stated that angiosarcoma can be expected to occur about 25 times in a year in a population the size of the U.S., and hepatoma is many many times more common.

CDC continued to work at the Louisville plant, collecting detailed information on cases that came to their attention and, within a month after this initial work, a fifth case was recognized by reviewing death certificates. The industrial consulting firm of Tabershaw and Cooper were performing a retrospective mortality study in all of the B.F. Goodrich plants and, using their data plus data which people at the Harvard School of Public Health had collected, CDC amassed lists of deaths at the Louisville plant in workers,

not just in the PVC unit. This is a plant that contained about 1,200 workers in all, of whom 270 at the present are engaged in PVC production. CDC collected death certificate information on 100. At the same time, in the Lousiville plant, the Company together with local authorities, were engaged in a detailed screening program to detect other latent cases of liver pathology. They started this program about September and, as of February, had screened everybody, about 1,200 employees in all.. From this screening, CDC was able to identify two additional cases of angiosarcoma of the liver. So, at present, from the Lousiville PVC worker population, these two new cases were PVC workers. No cases today were found in any of their workers working their synthetic rubber operation. There are seven cases of this rare tumor in just this one plant, said Dr. Heath.

One of the questions they had was whether this was a problem peculiar just to the Louisville plant. For quite a while, the only cases known were in the Louisville plant. But it has become apparent in the last two or three months, that this is indeed an industry-wide problem. Three other companies have recognized cases in their workers. (See Attachment III)

Practically simultaneous with the NIOSH-CDC investigation in Louisville, Dr. Selikoff, Mount Sinai Medical School, together with the United Rubber Workers, set up a study of the Goodyear Plant in Niagara Falls, N.Y. From this, to date, there have been recently identified three cases of angiosarcoma of the liver. The Union Carbide Plant in Charleston has one case, and the week of April 15, CDC reviewed slides of a man with liver tumor, on the chart called hepatoma, but considered by the pathologists, Dr. Thomas and Dr. Popper, to be angiosarcoma. So, the current case count is 12 cases confirmed. These cases are all in PVC polymerization plants. Some of these plants, in the past, had in their operation, monomer production as well. None at the present time have that kind of operation. Several of these men worked in monomer production in days passed, so their work histories are not completely in polymerization work. In fact, the work histories are quite involved. One cannot say that any one man has done one task specifically in the past nineteen years, for instance. They do tend to do all kinds of jobs in a polymerization plant.

Dr. Heath then made some points about these cases. Many were recognized only on autopsy. It is a very difficult diagnostic problem to identify these cases even after death. The average age of these cases is roughly 45, their duration of work with PVC is roughly about 20 years. The earliest case was diagnosed in 1962, a man from the Goodyear Plant in Niagara, about 40 years old, who had worked in various phases but did mostly monomer work for seven years. That is the shortest work history prior to the onset of illness.

Among the Louisville cases, there does seem to be a tendency for these people to work longer in these jobs. These details are very rough, however, and one shouldn't put a great deal of weight on them. This long duration and the fact that they are in a high exposure area does imply that these cases at least require high concentrations of VC exposure over long periods of time.

CDC just received the work history from the EIS officer who investigated the cases in Niagara. There is one man who is a confirmed heavy drinker, the rest are not heavy alcohol drinkers, so there is another question unanswered, Dr. Heath pointed out.

The most recent man interestingly enough gave a history of exposure to arsenical insecticides as a young man. Dr. Heath was not sure that the alcohol would tie in, but the arsenic, on the other hand, is pertinent because angiosarcoma has been described as a sequel to arsenic exposure.

One other case that has been talked about a lot is the one of the eight year old girl who is the daughter of a man who has worked at the plant for 10 years. Actually, prior to the onset of her symptoms, he had worked there only about 5 years. This little girl was diagnosed with hepatoma in 1971 and the slides were reviewed again at NIH and the diagnosis confirmed. We do not know exactly how close this family lives to the plant, we do not know the father's work history, only that he was a PVC worker. The question was raised as to how frequent is hepatoma in children. Dr. Richardson mentioned a study of New York City autopsy records by a Dr. Phillip at Memorial Hospital. This occurs in 1.6% of all childhood tumors under the age of 14. So it is a common lesion. Out of 137 primary malignant tumors, 23 were in children under the age of 14 years. There is no very distinct clinical pattern in these cases, said Dr. Heath. Liver function test abnormalities in many of these cases were so borderline as to be unremarkable. The current screen being used at Louisville is the SMA-12. NIOSH has since recommended to OSHA an additional liver function test as well as other recommendations regarding timing of testing, etc. The additional test is the GGTP (gamma glutamyl transpeptidase). (See Attachment IV)

The Goodrich people have done a great deal of screening, going through an entire plant, whether people were PVC workers or non-PVC workers. On the first testing, on the SMA-12 test, 25% had one or more abnormalities with the liver function test. This was the same picture that Dr. Selikoff and the United Rubber Workers found in their screening - a fairly high level of liver function abnormality. Of the 280-300 employees that had liver function abnormalities and went back for rescreening, 73 still had abnormalities. These they submitted to intensive liver work-up, including a liver scan, alpha-feto protein, etc., and a variety of liver function tests. Where there was a suspicion of abnormality on the liver scan, they were taken to an open liver biopsy following angiography. It was from this group of 73, that two people with angiosarcoma were diagnosed. In addition, in this

group, there are a number of men who on scan showed no liver abnormality, but showed a large spleen. These people are still not yet fully evaluated with respect to their liver performance. The question was raised whether anybody is looking at the angiosarcoma cases that are not associated with PVC production.

Dr. Heath has gone on to set up a surveillance project for angiosarcoma of the liver throughout the U.S., first by requesting death certificates from the National Center for Health Statistics, which was done in the early part of January. CDC is still in the midst of tracing down the death certificates for 1970. At the present time, CDC has 20 cases of angiosarcoma. These will be checked for pathology and the families will be contacted to get detailed information as to work history, etc. The second approach is more current - going after reports from individual pathologists. CDC has contacted a number of them and are putting notices in journals, etc., encouraging people to let them know if they diagnose any cases of angiosarcoma of the liver or if they have seen one in the recent past, so that CDC may be able to get back to that particular case to get a work history and exposure history, etc. This is another line of effort that CDC is just now getting into (See Attachment V) In the review of mortality in Louisville, the 100 charts that CDC has been able to trace of the 150 deaths that have occurred in this plant (that is known of), there have been to date 6 cases of brain tumor recognized, where 1.2 or 1.3 was expected. There are, perhaps, other tumors that might be increasing. There was a suggestion also that lymphoma might increase. The Niagara plant has two cases of lymphoma, one acute myelogous leukemia, it was believed, in workers in this plant. However, no cases of leukemia have been reported at Goodyear. There is the brain tumor suggestion, and also there is one case of nephroblastoma, (for what that is worth), in a worker that has worked at the Calvert City monomer plant which is still in the first stage of investigation. There are slightly more lung cancer cases than one might expect, but that is open to question.

Dr. Richardson mentioned that in Kentucky, there were a lot of brain tumors in one small area, which is a very interesting phenomenon. Dr. Kraybill thanked Drs. Wagoner and Heath for their excellent presentations.

The second half of the meeting was chaired by Dr. Bernard McNamara of the Toxicology Division, Edgewood Arsenal, who introduced the next speaker, Dr. Raymond Shapiro, Bureau of Foods, Food and Drug Administration.

Food and Drug Administration (Bureau of Foods)

Dr. Shapiro began by saying that within FDA, each bureau concerned with vinyl chloride has set up a small group of people to concern themselves with this problem. Dr. Shapiro co-chairs the Bureau of Foods Team. The

Commissioner has set up an inter-bureau liaison group under Dr. Shaffner, which meets as often as necessary, and has had two meetings so far. The Bureau of Foods interest was discussed by Dr. Shapiro, with Dr. D'Aguanno discussing the Bureau of Drugs position (next section). Basically, there are two areas, the inhalation problem and the migration problem. The inhalation problem is the use of vinyl chloride as a propellant, primarily in the cosmetic area, with some use in the drug area. There has been a recall of all vinyl chloride propellant-containing cosmetics on the market. This recall is at the retail level. A document has been prepared, which will eventually appear in the Federal Register, to ban the use of VC as a propellant in cosmetics. In actuality, there has been no use of VC in the packaging of cosmetics since June, 1973. In the drug area, he believes, there will be an effective banning of VC as a propellant by labeling it as an NDA. Industry would have to come in with an NDA to get VC used as a propellant, which would not be granted. This, in essence, accomplishes the job. In the migration area, there are three separate areas under consideration: one, the container aspect in terms of cosmetic products packaged in PVC containers and potential migration of the monomer from the container to the cosmetic product; there are food containers which might present the possibility of migration from the container wall into the food product therein; and then, there are the film wrapping materials used in packaging foods. Again, that is a problem of migration. FDA is developing a position, at least in the Bureau of Foods, for these three situations which will set, as an interim, a proposed level of monomer in the packaging material and a proposed level of monomer in the food that is being contained, not to exceed a certain level in the foods. These will be purely interim standards until oral toxicity can be developed. Depending upon the nature of the oral toxicity data, one would, if it were a non-carcinogen, probably set levels of intake based on the animal data. If it is a carcinogen, then there is an entirely different legal situation. These documents will be published quite shortly in the Federal Register outlining FDA's position.

Food and Drug Administration (Bureau of Drugs)

Dr. William D'Aguanno then covered the Bureau of Drugs effects. The extent of the problem in the drug area seems to be not well-defined at this time. It is known that the survey made for aerosols to determine what was being used as propellants, picked up one company that used VC. It was a small volume company that used VC for the room sprays of decongestant type materials. But, as pointed previously, as of June of last year (1973), VC was no longer used as a propellant. This company has had seven drug products with 16 formulations and five cosmetic products which they marketed with VC as the propellant. The Bureau of Drugs has forwarded a recommendation to the Commissioner to the effect that any aerosol or inhalation product in which VC is used as a propellant or ingredient would be a new drug and anyone who is marketing it without a new drug application (NDA) approval would be subject to regulatory proceedings. As far as the packaging material, Bureau of Drugs is asking for information under two phases, (1) under the Drug Listing Act, which calls for certain pieces of information that must be complied with, and (2) the other one is a voluntary request for information. Bureau of Drugs does have a number of products which are new drugs by virtue of the container, that being the large volume parenterals which are polyvinyl chloride bagged.

Bureau of Drugs is checking on what is available in terms of information in the Drug Master Files and the NDAs and ultimately will get in touch with those companies also. The Bureau of Biologics obviously has the same problem with the blood bags that Bureau of Drugs has. They are a drug problem because they have ACD in it, the anticoagulant, but then after the blood gets added, they become a problem of the Bureau of Biologics. So, we have a common problem, but since the manufacturing controls are basically in the Bureau of Drugs, Bureau of Drugs will probably be more intimately involved.

The question was asked whether any leaching studies have been done on any of the blood bags. Dr. D'Aguanno indicated that the Bureau of Drugs' main area of concentration on the blood bags, up until now, has been on the diethylhexylphthalate problem. There is some material on leaching studies on certain packaging materials in the Bureau of Foods.

Dr. Shapiro felt that there are two problems in getting a data base that will be adequate. Most of the methodology that is being used has involved mass spectroscopic confirmation. However, the actual data that has been derived does not necessarily involve this method and, in order to close the loop, one has to be sure that one is not measuring an artifact. This will be the first question that someone will ask: could there be an artifact that could have the same GLC peak that might be in the material that is leaching out the monomer? In data that Bureau of Foods has been able to put together, whereas the methodology is laboratory validated and mass spectroscopy confirmed in the actual samples themselves, VC may not have been confirmed even on a selective basis. There is another problem in that the data obtained is only going to be relative to the sensitivity that has been applied. Thus, some of the crudity of analysis introduces some apparent negatives which may not be negatives, in fact. There was a Federal Register document of last May (1973) on the polyvinyl chloride containers for alcoholic beverages. The leaching of VC monomer was something in the neighborhood of 10 to 20 ppm in the alcoholic beverage. That was the time they were taken off of the market. Bureau of Foods has some food data going as high as 6 ppm, but again, confirmatory data is needed.

A question was then raised as to what happens in the heat treating process. Dr. Shapiro mentioned the meat wrappers syndrome, a respiratory problem which is out of FDA's area of responsibility. This might be a hydrochloric acid situation or it might be vinyl chloride or some other degradation product. NIOSH and OSHA are certainly looking into it. Then there is the actual physics of when the material is wrapped and is sitting on the counter. What is the migration as a function of time in shelf-life? There is also the case of short-term wrapping in a heat environment. If this involves migration into the food, then the responsibility will be with FDA. FDA has not initiated any ingestion studies. It is very possible that industry has initiated these studies on ingestion and that they may be well advanced, but for proprietary reasons, they would not be required to divulge this information until these studies are completed. Industry has been told that they have the number of years that it will take to develop the data. Therefore, the

FDA standards that will be proposed in the Federal Register are purely interim standards until the data base is developed or further data develops in other areas that would indicate differently. Dr. Maltoni, in essence, has a feeding study, although Dr. Shapiro personally believes that it is a gavage study from the brief description of it. But it is an oral type of exposure in olive oil and is about 2 months old by now, from the very cursory report that was given. The question was raised why March 1973 was the critical date. Dr. Shapiro replied that the Maltoni data base was developed and paid for by a consortium of companies in Europe. One of them was ICI. The document Dr. Maltoni brought to the U.S. was written with a date of February 5 and was presented on the 15th of February. If one goes back 9 months, and notes the first tumor appears at the highest level, which was recorded as an angiosarcoma. This awareness of tumor formation from VC was strong suggestive evidence to industry and could suggest action on shipping.

Dr. Shapiro indicated that it was very likely that industry knew what was going to happen around March and then started to form their posture. The question was asked what FDA would do if the oral studies were negative and the migration was positive. Dr. Shapiro answered that the migration is positive, but this is not debatable, but a fact. If the oral study were negative, FDA would probably be legally obligated to regulate it on the no effect level of the oral study. If a well-documented, well-performed oral chronic toxicity study showed no carcinogenicity, FDA would then regulate on the basis of the classical approach to a food additive. At the present, it is going in as an interim food additive listing on an emergency type basis. It was mentioned that if one would make a statistical extrapolation of the Maltoni rat data at the 2,500, 1,500, 500 and 250 level and then wanted to get down to 50, with two or three hundred animals, he might have picked up angiosarcoma, but not with 64. So, if these other values that are becoming available with mice are positive with a zero colony at the 50 ppm level, it is not inconsistent with Maltoni's studies. There is a species strain difference. Dr. Shapiro mentioned that industry has the responsibility to validate the safety of any food additive in use and FDA has the legal prerogative of demanding that data. If you are looking for a solid study with adequate numbers and adequate approach, a 2½ to 3 year time frame is involved. One has to be also certain that the VC orally administered is really what one is administering because one is dealing with a gaseous phase and administering it orally. Maltoni puts it in olive oil and gavages. The question is whether we would want to put it in olive oil and then mix it with the food.

Dr. McNamara then introduced Dr. Mehlr, who was attending in place of Dr. McLaughlin. Dr. Mehlr is Director of the Bureau of Biological Sciences in the Consumer Product Safety Commission.

Consumer Product Safety Commission

Dr. Hehir indicated that CPSC in February of this year made an inquiry of industry to find out what the scope of the problem was as far as the Hazardous Substances Act as statutory authority is concerned. As most of the people know, CPSC had transferred, at the time they became a Commission, four acts: the Hazardous Substances Act, the Flammable Fabrics Act, the Poison Prevention Packaging Act, and the Refrigerator Door Safety Act. At this moment, CPSC is concerned under the Hazardous Substances Act with those products which are not foods, drugs, cosmetics, or economic poisons. CPSC was told, in a very general way, that industry had stopped using voluntarily some time ago and that they were fairly certain, about 90% certain, that most of the industry was not using VC. They would not, however, be aware that some small packagers may be using VC. In order to find out what the situation was, they made further inquiries and found there are some potential areas where VC might be used in household products. Just because it is not a food, drug, cosmetic, or economic poison, does not automatically classify it as a hazardous substance. It, first of all, must be classed as a hazardous substance to be subject to CPSC regulation. From what has been said about the toxicology of VC, there is some agreement, at least among experts, that there is a problem. So, what CPSC is doing at this time is proposing to ban VC as a monomer in a propellant system that would be utilized as a household product. CPSC will allow 30 days to show cause why they should not do so. Secondly, CPSC is requesting information, and thirdly, they would like to know the trade name of the products of those household ingredients that presently have VC and those which contained it in the past. That is basically what they are doing. There are a number of ways CPSC can move: injunction, banning, seizure, recall, etc. For example, to classify something as a banned hazard indicates that labeling at one time was considered adequate. At this point, a banned substance indicates that the labeling per se is not sufficient to protect the public health and CPSC would institute a recall immediately. But prior to doing any of that, CPSC is proposing (the Federal Register statement went to the Commission on April 17) to ban it but to allow adequate time for comment.

The question was asked whether PVC plumbing materials come under the jurisdiction of CPSC and the answer was that architectural structures and things of that nature do. It is a kind of joint venture with EPA. Plumbings, pipes, or any asbestos filters that go into the household do come under CPSC. CPSC would only ban a substance for household use, not for industrial use. CPSC has alternatives other than banning, if so indicated. Something can be banned as a hazardous substance or as an imminent hazard and the actions taken under these remedies are entirely different.

If, for instance, VC is used in a paint which is used only by professional painters, then the problem belongs to OSHA, but if it is used in a spray paint used by the home owner, then CPSC becomes involved. Spray paint is one of the areas that CPSC is concerned about.

CPSC works very closely with the other regulatory agencies and has been in touch with OSHA, NIOSH, FDA, EPA, etc. The agencies, in turn, keep CPSC abreast of what is going on.

The proposed CPSC announcement in the Federal Register includes, as a banned hazardous substance, VC monomer as a propellant or an ingredient in the propellant. CPSC is therefore concerned with VC primarily as a propellant system. But it is also used in specialty coatings.

Since CPSC has no pre-clearance, it has no way of knowing how many products contain VC at this point in time, nor in the past. CPSC has asked and surveyed industry. In case industry does not want to cooperate, CPSC can subpoena that data. The Consumer Product Safety Act makes that provision but CPSC has to have a reason for asking for the data.

Dr. Shapiro indicated at this time that by the end of the week of April 15, 2,600 registered letters will have been sent from the Bureau of Foods requesting information from various industries.

Mrs. Williams (Department of Transportation) indicated that DOT proposes in the Federal Register to classify a material as a hazardous substance, then it is up to industry to prove that it is not.

Dr. D'Aguanno then chaired the next portion of the meeting and introduced Dr. Nancy Beach, who is coordinating EPA's activities on VC.

Environmental Protection Agency

Dr. Beach indicated that, in response to a report of considerable loss of VC into the environment during the manufacture of PVC, EPA became concerned about the environmental health risks outside the work place. An agency task force was established to assess the risks that are associated with the manufacture, distribution, and disposal of both VC and PVC. Dr. Beach continued by describing EPA's mandate which includes primarily the disposal of all wastes, gaseous, liquid and solid, the drinking water standards, and the registration of pesticides. EPA has no jurisdiction over the work place except with respect to the disposal of wastes into air, water, or land. They have no authority over food, cosmetics, or drugs, except for disposal of wastes containing these items. Early industry reports mentioned a 6% loss of VC during polymerization. EPA's task force is investigating this and it appears that while the loss of VC can vary from plant to plant, depending on the age of the plant, the polymerization process being used, and the capacity of the plant, the 6% loss figure is a good one. It sounds small, but if one considers that the annual production of PVC in the U.S. is well over 5 billion pounds, a 6% loss figure is on the order of 250 million pounds, which is somehow getting out of the work place. The task force has

requested from the EPA Regional Offices monitoring activities around the VC and PVC plants. To date, EPA has very preliminary data on the air and waste water levels of VC around the B.F. Goodrich plant in Louisville, Kentucky. The Monitoring Team from Region IV, which is headquartered in Atlanta, did not enter the plant proper. They measured the levels of VC in air from the plant boundary up to 3 miles away. Levels in the parts per million range were detected up to ½ mile away from the plant boundary. The highest level detected was 2 ppm right at the edge of the plant. This data is very preliminary and the task force is evaluating the detection techniques and sampling techniques and, hopefully more definite data will be available at a later stage. EPA is also looking into the report of a daughter of a worker at the B.F. Goodrich plant who has a hepatoma, because EPA is concerned about the possibility that workers may be carrying dust home and that there may be an exposure in the home. This is one of the reasons that the task force perhaps should be looking into the angiosarcomas of the liver in the population beyond the workers. EPA, however, has no activity in this area. EPA does have a nationwide monitoring effort related to the PVC plants. The location of the PVC plants is known and the regional offices have been asked to measure levels in the ambient air and in waste water streams. Measurements of waste water from the B.F. Goodrich plant revealed 2 to 3 ppm of VC at the discharge point. The municipal water supplies will be checked for a possibility of VC getting through into it.

The question was asked by the Chairman if there may be something expected from the aquatic life, a point source contamination such as in catfish, etc. Dr. Beach replied that fish kills have been reported from the disposal of VC-generated wastes in the North Sea, but at this time, it is really not known how long VC remains in the water effluent. Also, the toxicity is very low. The task force is also looking at disposal of solid waste into municipal systems and present figures indicate that PVC is .3% of the total solid waste load or about 1 million tons per year. EPA does not know the products in the solid waste from the PVC plants, but knows what the disposal methods are; namely, incineration, land fill, and deep well injection. EPA's Office of Solid Waste Management is looking into the dangers from leaching and the products which result from combustion. Thus far, only the loss from polymer manufacture has been discussed. In addition, there is accidental exposure to VC resulting from spills during transport. Industry has reported that about 75% of the monomer produced in this country is transported away from the site of production, mostly by rail, a very small percentage by barge. So, the very distinct possibility exists that there may be increasing exposure through derailments. In the past three years, there have been approximately 10 accidental VC spills, most of these being tank car derailments. The most recent one occurred on April 15 in Philadelphia. EPA is also looking at the uses of VC beyond the polymerization process. Approximately 97% of total monomer produced in this country is used for the polymer, but the remaining percentage goes into three areas: (1) for the production of methyl chloroform, (2) another for an additive in specialty coatings, and (3) for aerosol sprays. EPA is also concerned about import of VC and how it is coming into the country, either as unprocessed monomer or processed

monomer. The most controversial item in EPA at the moment is the petition from the Nader group (Health Research Group) to the agency to ban pesticide sprays which contain VC as a propellant. In addition, they have asked for publication of all of the brand names of all of the pesticide products containing VC as a propellant. Fortunately, unlike FDA and CPSC, EPA does have a pesticide registry and all manufacturers have to register with EPA their formulations. These are coded, of course, because they are considered confidential. EPA has searched that register and has the names of 41 pesticide products which contain VC. The manufacturers have been contacted and asked whether they had any objection to the release of the brand names and today (April 17) a press release is going out with 20 brand names of pesticide products that contain VC. Three base manufacturers and seven distributors did object to the release of the brand names, but the names of the manufacturers and distributors will be published to satisfy the Health Research Group's petition. EPA also has a research activity at Research Triangle Park, N.C. in measuring the disappearance of VC resulting from a pesticide or hair spray sprayed into a small chamber, approximately the size of a bathroom, to determine how quickly it disperses and the levels decrease. What is really needed are low level toxicity experiments. EPA has been meeting with industry. The task force met with the Manufacturing Chemicsts Association and also with public interest groups and have scheduled future trips to both monomer and polymer plants.

National Cancer Institute

The next speaker was Dr. David Levin from the National Cancer Institute who presented the work in the Field Studies and Statistics Area, in the Division of Cancer Cause and Prevention. Two of the main activities involve large scale epidemiology-demography type of studies on large populations. The first one is the Third National Cancer Survey. This is now being completed and is a survey of all new cases of cancer diagnosed in an area approximately 1/10 of the total U.S. It includes the entire state of Colorado, the entire state of Iowa, Detroit, Minneapolis, St. Paul, Atlanta, Birmingham, Dallas, and the San Francisco area. This is a population-based study, the population of those 7 cities and 2 states is approximately 1/10 of the total population of the U.S.

All new cases diagnosed between 1969 and 1971 have been recorded so their incidence data is based on a three year span. Over that three year period, 8 cases of liver cancers have been reported. These include hemangioepitheliomas, hemangioepitheliosarcomas, and one hemangiopericytoma. Based on these 8 cases: 8 cases over three years in the survey area multiplied by 10 equals 80 cases over three years in the total U.S., divided by 3 is a figure of 27 cases a year in the U.S.

Of all of those cases, one was exposed to thorotrast and two cases are in children. So, if those three are eliminated, it leaves five cases which may be comparable to the exposure in the PVC workers. None of the areas surveyed match the area where the PVC plants are. That is the available incidence data. In addition, there is information from the End Results Group. The End Results

in their latest report, "summarizes the experience of more than 100 hospitals of various types and sizes and different parts of the U.S. The extent to which the institutions participating are representative of all hospitals and clinics in the U.S. is not known. They do, however, represent a very broad experience and provide a bases for examining trends in cancer therapy and patient survival."

From the End Results Group, one cannot get incidence data because one does not have a denominator. One does not know the population. What is known, however, is that there are over 600,000 reported cases in the files from 1940. The current report, End Results No. 4, covers the period from 1955 to 1964 and in that period there are approximately 200,000 cases. Of all of these cases, after a records check, there are 22 cases of liver hemangiomas, etc., in that whole category. The first one dates back to 1942, there were 7 cases between 1955 and 1964 and an additional 9 or 10 cases from 1965 until 1971. These cases are ones that have been reported and have come into the hospital and have entered the systems. There are some restrictions on that. People who have had prior therapy for their tumors are not in the system. The system is based on measuring treatment and survival, so what is included are cases that have come into the hospital, essentially new cases without prior therapy, and have then been followed.

The Head of the End Results Section stated that he really did not feel there was a great increase in incidence but it must be remembered that the population on which these cases are drawn has been changing all the time. They are listed in chronological order, but are really not indicative of a time frame. The cases from Third National Cancer Survey have been discussed and coordinated with Dr. Heath (CDC) and NICSH. There is some problem with confidentiality. In order to collect the data on these people, NCI cannot reveal it. But NCI is working through CDC, having them contact the physicians to see if they can get detailed information on the patients. Specific details are not available to NCI on these cases since most of them were from death certificates and hospital records. These do not involve occupational history and things of that sort.

There is one other activity going on in the Epidemiology area. One of their researchers is doing a survey of liver tumors on a county-wide basis. This work is just being set up and there have been no conclusions drawn as yet. In 1937, there was a 10 city survey done. In 1947, there was another survey which was called the Second National Cancer Survey. The Third National Cancer Survey is kind of a result of the Second. One of the things decided on the basis of that was that this was not the way to do it. Field Studies and Statistics is now putting together essentially the end results system and some of the survey areas in what is called the SEER Program (Survival, Epidemiology and End Results Reporting). Contracts have been let with many registries (9), which are going to be collecting data on a continuous, ongoing basis, on a population-based registry, in order to get continuous monitoring of incidence, survival, and results, and all of those things that were done previously on a one-shot basis.

Special Panel on Pathology

Dr. Richardson took over the chairmanship for the remainder of the meeting and made several comments on epidemiology and pathology. (He indicated that he practiced pathology in five different states.) He stated that invariably, when you go in to perform an autopsy, you have to sign the death certificate so that the body can be moved and buried the next day. In essence, he pointed out many reasons why the death certificates are not reliable indices for final factual reporting on pathology.

Prior to 1947, and this is verified by Dr. Selikoff, the New York City Cancer Registry had 78,000 autopsies and one liver angiosarcoma. The Los Angelos tumor registry had 52,000 autopsies with one sarcoma. The Cook County hospital group, who are always talking about their arsenical carcinomas and angiosarcomas in liver, from 1951 to 1970 out of 39,000 autopsies, had 5 liver angiosarcomas, two or three of these are thorotrast-induced and two or three of these they claim to be arsenic-induced. They also claim that some of these are due to naccrsphenamine. Terminology on this lesion completely ruins the computerized system. Listed in the handout are 15 different terms for the same lesion, angiosarcoma. This was the most controversial lesion in the U.S. and also in the British Empire.

Dr. Richardson then discussed his summary, a copy of which is attached (Attachment VI).

At the present time it is estimated that there still are cases of thorotrast hepatomas and angiosarcomas in the population and an article reviewed by Dr. Richardson (in Minnesota Medicine) demonstrates that there are approximately 50,000 to 100,000 carriers of this radioactive media still present in our population. Dr. D'Aguanno indicated that, as far as he knew, thorotrast was still approved. He did not think that the NDA had been withdrawn on it, but there may be severely restrictive labelings on it. Dr. D'Aguanno does not remember the name of the company, but thinks it goes back to 1964 or 1965.

Dr. Richardson continued with a discussion of arsenic. Arsenic is one of the most controversial subjects that one can ever read on, mainly because there has not been an animal model that responds to it. However, there is quite a bit of material in the literature on arsenic tumors produced, not only on the skin, but at various sites in the internal organs. The angiosarcomas, however, in the liver have been produced in the vineyard workers in not only Germany but also in France. The man who wrote up most of this was Roth in Germany. He reported a total of 8 angiosarcomas of the liver due to the arsenical pesticides spray that was used in the vineyards. The case of Fowler solution, which is referred to by everybody, is in 1968 by Regelsen and in this particular case, the person took Fowler solution or arsenic with an induction period of 17 years plus 7. So each of the arsenic cases have had a long latency period. The vineyard workers are exposed 12-17 years,

with an estimated exposure of 52 grams, and the Fowler solution also the same length of time with an estimated exposure of 50 grams. So apparently, they had to take a lot of arsenic. Now, another thing came to the picture that is interesting. Arsenic is present in the Taiwan drinking water and, also in Taiwan, 19.5 percent of all male cancer patients in the hospitals for the last ten years have had carcinoma of the liver. The type, or what the histologic morphology and classification, has not been published. Dr. Richardson has contacted Dr. Lu (WHO) by mail for information on this.

Another item reviewed by Dr. Richardson is hemangioendotheliomas in infants. This would be the same thing as angiosarcomas. In 1961, F. Stout reported one case of liver sarcoma and in 1969, a fellow by the name of Bloomfield reported 36 cases with multiple liver hemangiomas or angiosarcomas in children, all died within 6 months. So, here is an incidence in the literature that should be looked at more closely. In animals, there is a spontaneous type of angiosarcoma in the hairless mouse. Dr. Derringer at NCI did the work on this lesion. At the Eppley Institute in Omaha, Nebraska, a report claims there is approximately 5% angiosarcomas with the Swiss strain mouse. Listed in the handout are the various hydrazine compounds that have been used to produce angiosarcomas and also the urethane compounds that have been used, so one wants to look at this whole picture and can easily see that this is probably just the tip of the iceberg that is coming up in the future in the environment. What is badly needed in this nation is a central registry for chemicals in the environment and chemicals that are being used industrially. Several years ago, we foresaw this and requested EPA to consider this registry with the Armed Forces Institute of Pathology, since they have the greatest number of expert pathologists. Dr. Richardson made the plea for coordination in this area and the need for central repository. There has been much dissemination of registry material in the last few years. Dr. Pallota indicated that Toxic Substances Control Act, (Dr. Pallota is with EPA) that has passed both the House and the Senate and is in conference, has a provision which requires the registration of all of the chemicals that are being produced.

Dr. Richardson briefly mentioned renal cell carcinoma of the kidney in children. Up until 1934, renal cell carcinoma in children was controversial. However, by the year 1973, there are a total number of 59 cases reported in the English literature.

Another point mentioned is that there is suggestive evidence from Professor Maltoni's work that one should be looking for kidney tumors in the human population from chemical exposure.

Armed Forces Institute of Pathology

Dr. Q.A. McAllister: "I was asked simply to show you what an angiosarcoma looks like.

Slide: "In the combined registries of Cardiovascular Pathology and the Hepatic Registry, we have 66 examples of angiosarcoma of the liver not associated with thorotrast and I will confine my comments to those. Of the 66 that we have, 66% have multiple nodules scattered through the liver.

Slide: "The gross appearance is one of gross lobulation that can be palpated by the clinician, probably too late to do the patient much good.

Slide: "Although 66% did have multiple nodules, others were large solitary nodules, sometimes in one lobe of the liver, with apparent gross sparing, and we will get to that in more detail later - of the other lobe. Briefly, the lesions are very hemorrhagic and you can see the comment that was made earlier of rupture and hemoperitoneum in the rats - and that can quite easily occur in the human being as well.

Slide: "It has been said, in the literature, that angiosarcoma is associated with cirrhosis. A very quick perusal of our material showed that only 13% of the patients had cirrhosis. This is a cirrhotic liver, a large focus, perhaps multifocal, angiosarcoma; sections of the spleen, you can see fairly large areas of angiosarcoma in the spleen and two or three other areas. If I had a large spleen and had been exposed to vinyl chloride, I would certainly want a spleenic scan on this basis and perhaps even a spleenectomy. An emotional comment, not a scientific one, at this point. Curiously enough, those patients that we had - the 13% of the 66 that did have cirrhosis, ten of them had portal of Laennec's cirrhosis. One was a child, about 2 years old, of Chinese extraction, that had biliary cirrhosis. None of them had post-necrotic cirrhosis or hemocromatosis, the types we associate mainly with hepatocellular carcinoma.

Slide: "The microscopic picture of angiosarcoma of the liver is much like angiosarcoma elsewhere. That is, they vary in appearance. The most classic, the most common we see, is like this. Hepatocytes scattered about, compressed, they lose very often their characteristic picture and are replaced by fibrous tissue. Fibrous stroma is very common in angiosarcoma anywhere in the body. The dark dots on the slide are the nucleii of endothelio cells which vary in size, shape, and chromaticity, tufts grow autonomously into vascular channels; very commonly, areas of necrosis and hemorrhage into them - angiosarcoma.

Slide: "You can have angiosarcoma in the liver with disruption of the architecture and with cells that are somewhat hyperchromatic, dark, protruding, angry-looking, but then they pile up, vary in size, shape, and chromaticity, tufted into the endothelio channels.

Slide: "Or you may find some that may be confused, superficially, with a metastatic adenocarcinoma in that the nucleii, instead of being very dark and angry, are very open with clear spaces and angry looking, but the chromatin pattern is ragged and jagged, all of the signs of neoplasia - again another phase of hepatic angiosarcoma.

Slide: "We see transitional forms. If you get the diagnostic open area of angiosarcoma, there is usually not much of a problem in diagnosis, although we too get them diagnosed as hepatoma or hepatocellular carcinoma. Coming away from the area, these cells we see here are Kupffer cells. These are the plates of the liver, the hepatocytes. You can see these cells rounding up, getting angry, and protruding into the lumen. This would still be, by our criteria, angiosarcoma, or we may call it probable, and wish we had more tissue.

Slide: "Not uncommonly, however, as one gets away from an area of active, diagnostic angiosarcoma, even into the other lobule of the liver, we will find areas where we have hepatocytes with an intact reticulum and the cells on the outside, the Kupffer cells, are darker than usual, and more prominent. Dr. Ishak (Dr. Kamal Ishak, Chief, Hepatic Branch, AFIP) likes to refer to this as sarcoma in situ. That is debatable. But what are they doing? Are we dealing with multifocal disease? Are these reactive? I don't think so. It probably is a multifocal disease as well as a metastatic disease when we see these multiple nodules.

Slide: "And again, away from the lesion, in the outer lobule here are your hepatocytes. These Kupffer cells are prominent, they are beginning to vary in size, shape, and chromaticity, their reticulum is not disrupted; they seem to be behaving themselves but they seem to be curious about misbehaving tomorrow. I can't say 'take a two-dimensional structure and compute a time dimension into it', but these lesions may well progress into angiosarcoma. The question that we come about is if you have a patient exposed to vinyl chloride, if this is a reversible lesion - he comes in with an abnormal liver function, it goes away - and he had this microscopic pattern, is this reversible? The question is not answered.

Slide: "Again, just like in any other tumor, angiosarcoma of the liver has many faces. I have shown you the most characteristic patterns. Others may look like this, just like angiosarcomas anywhere else in the body. Why should we suspect this one to be that different? They may often go into a solid phase with more cytoplasm, again with the nuclear criteria of malignancy, many mitoses, necrosis, a more solid form of angiosarcoma of the liver.

Slide: "A high power view showing the difference in size, shape, and nuclear staining properties, again, in other areas this formed very distinct vascular channels. You could see continuity with abnormal Kupffer cells going through the ones we just saw, at the periphery of the lesion. We consider this to be an angiosarcoma.

Slide: "Like angiomatous lesions in the skin, the gut, the lungs, anywhere else, very often there will be a sclerosing process and you see a lot of connective tissue being deposited between the malignant cells. Beware of the pathologist who will diagnose cirrhosis because of this fibrous stroma of the liver. Very often it may well not be.

Slide: "And again, a dense hylinized collagen between the malignant cells, not cirrhosis at all. Looking at the liver away from this malignant nodule there was absolutely no evidence of cirrhosis.

Slide: "Curiously enough, bringing the question up again of the multiple nodules in 66% of these. Are they metastatic with one primary or is it a multifocal lesion? In hemangiosarcoma of the liver, we not uncommonly at all, if we look hard enough, will find portal veins with the malignant cells lining where you would find normal endothelium lining the vascular channels. Not a tumor plug sitting in the vessel as you might see in hepatocellular carcinoma but they are actually lining part of where we would expect to find normal endothelium. It appears to be, just superficially, and I reserve to right to retract this, it appears to be a stimulus that takes place and causes this proliferation of Kupffer cells and endothelial cells in a very extensive way.

Slide: "As far as metastates go, in autopsy cases that we had, 45% had metastases into other sites of the body. The most common sites of metastases were the local lymph nodes, especially those in the porta hepatis and around the pancreas, the lung, and the spleen, and a very high percentage in the bone marrow.

Slide: "This is a sectioned spleen, stained with H&E, and again you can see the vascular channels lined by these angry cells - angiosarcoma, be it in the liver, lung, spleen, or whatever."

Dr. Richardson thanked Dr. McAllister for a very excellent presentation and indicated that he had just reviewed Dr. Stewart's slide of angiosarcomas in animals and that they are almost identical.

Dr. Richardson then introduced Dr. Hans Popper (NIH Fogarty Scholar) who has been the center point with Dr. Louis Thomas of reviewing the cases of viryl chloride workers that have been sent in from Louisville.

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

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: All Interagency Collaborative Group on Environmental Carcinogenesis Members and Liaison Addressees June 26, 1974

: Chairman, Interagency Collaborative Group on Environmental Carcinogenesis

: Dr. Hans Popper's Presentation at Vinyl Chloride Meeting April 17, 1974

1. Attached is the edited transcript of Dr. Hans Popper's (MIH/FIC) vinyl chloride presentation at the April 17 meeting of the ICGEC. Please detach pages 24-27 and replace with the enclosed material. Thank you.

H.F. Kraybill, Ph.D.

Attachment

Dr. Popper gave a brief summary of how he became interested in liver disease. He also noted for the record that he is an "a pathologist at Mount Sinai and presently at NIH as a Regents Scholar on sabbatical, which is the reason why I am looking at this matter from a different viewpoint and that is the reason why I want to acquaint you with that viewpoint. NCI (Dr. Thomas) received [illegible] NIOSH (Dr. Smith and Dr. Creech) some material and we looked at it. Now [illegible]s are angiosarcomas, and I don't think I shall waste your time now to show you pictures to compete with the very excellent presentation by Dr. Wahlister.

"Two things happened. I have been notified by people in Germany, with whom I had contact about alcohol, that they have observed a large number of cases which they thought to show, although they were not clear, some hepatic fibrosis in vinyl chloride workers who were cleaning the autoclaves, as they call it. That is the same as you are calling your vessels or vats. These workers developed, and this is an interesting relationship, acroosteolysis and had therefore been checked by the Dermatological Department of the University of Bonn. I give a lot of credit to dermatologists to recognize large spleens. These German dermatologists were fascinated, so they sent these cases to an internist. They wrote to me of these cases and their notification of vinyl chloride injury came two days before Dr. Thomas showed me the pictures of the four cases of cirrhosis. So, obviously, I was already alerted. These four cases of cirrhosis, delivered to us as alcoholic cirrhosis, turned out to be a fascinating lesion. I think in what little time we have, I will describe it to you because it really is the crux of the matter.

"I am slightly disappointed that really no one has emphasized this lesion because it is the kind of lesion you should search for. At least in one patient we know, he has recovered from this kind of lesion. I think, from a public health standpoint, that this is a far more important element than the angiosarcoma in which, I am afraid, not much can be done.

"What is this lesion? The liver has a very characteristic surface. The Germans do a laparoscopy, then see a diagnostic picture. It is a peculiar surface scarring which is very much on one of the entities which we [illegible] here, alerted by this German picture. We do not see this kind of [illegible], except that one was seen the other day here at the Clinical Center. The second important feature is that in the liver biopsy [illegible] we see portal fibrosis, [illegible], and we see a kind of [illegible] fibrosis. [illegible] at the liver. Usually [illegible] it is, I am not sure that I would diagnose it as a [illegible]. I [illegible] portal and [illegible] one has to look [illegible]. [illegible] [illegible] [illegible] liver, [illegible] [illegible] [illegible]

"Many of you who are older in this room will remember the terrible name 'Banti's Syndrome'. When I was young, we used the term Banti. As a matter of fact, I saw that old man 50 years ago. I saw the original Banti spleen. My then chief got from Banti, in Italy, the spleen. It is still in the safe. The spleens are quite characteristic. They are in congestive cirrhosis and hemangiomas in cases. They have very large lymphfollicles, so there is some kind of lymphoid infiltration and they have lymphocytes around the lymph follicles, just like Banti's spleens, and that means an acute portal hypertension.

"The Germans have some 50 cases of that type. Now, in their cases they saw, for the first time, a peculiar hemangiomatous nodule in the liver (i.e. angiosarcoma of the German vinyl chloride polymerization), which they did not dare to biopsy because of danger of bleeding, probably an angiosarcoma. So, what does this mean? They have probably seen widespread lesion which looks like Banti disease and eventually become angiosarcomas, or a few may become carcinomas.

"Now, why do I say that? We have two cases of carcinoma in the whole group, real carcinoma, not to speak of the child. One case at Mount Sinai, which Dr. Selikoff sent in, and we actually have this patient here. In this case, it is unquestionably a carcinoma because in the rest of the liver, the changes are suggestive of just that. There is a second case that is apparently proven, not in the Kentucky cases, but the Hungarian cases. A good pathologist has called it carcinoma, but we have not seen it yet. So there is surely a chance for carcinoma, not to speak of the child, the 5-year-old girl. Therefore, if any screening is done, I think you should look to pick up the precursors. One of the four cases which we received from Kentucky was admitted to the Clinical Center here at NIH and is still here. We have seen the liver on biopsy. He had thrombocytopenia and a splenectomy. The liver picture now is normal. The liver function tests that were abnormal now are normal, and the liver looks normal except for terrible surface adhesions. He has been away for two years from any exposure. You can't make one case a story, but I would still like to consider the fact that there exists, without a doubt, a precursor lesion which should be picked up.

"The last remark: An organic arsenical produces exactly the same lesion in man. There are cases reported - two cases and they became a third one. Fowler's solution for psoriasis produces this picture of hepatic fibrosis, portal hypertension, splenomegaly, the same as the Banti-type syndrome. They liken that liver and the picture is internally comparable with our cases. So arguably, there are situations in which the environmental factors, and especially our chemicals, play a role. And again, I have no [illegible] that this is true [illegible] vinyl chloride. It may be [illegible] which [illegible] should be [illegible] they did. We [illegible] under the [illegible] were, [illegible] can't they report it to the [illegible] cases. [illegible] [illegible] [illegible]

"not go into any detail. I am raising the question that, just like with primary hepatic carcinoma, there is a correlation which, not with alcohol but with viral hepatitis. Now, this may be a red herring, but the fact that cases in Australia have Australia antigen. At the present time, Australian antigen can be determined almost as readily as twelve-channel SMA. I think we should consider these possibilities. Certainly, we all know that, in certain parts of the world, i.e., Uganda, Taiwan, etc., the incidence of Australian antigen in primary hepatic cancer is very high.

"Now then, the arsenical cases in Germany unfortunately are lost. I happened to be in Bonn and I wanted to see the arsenic cases. Dr. Roth, whom you referred to, moved to Berlin and everything is lost. But there are cases of arsenical lung cancer in this country, for example, in Colorado, and I am just now trying to get those livers. I think I have said all that I want to say."

The question was asked whether the precancer lesion can be reversed. Dr. Popper replied that if they have thrombocytopenia, they would take the spleen out. In none of them, they did a partial excision. He said that he would not do this. "The most important thing is to take them away from exposure. The gentleman I am referring to is a 28 year old worker that Dr. Roth and Dr. Creech sent in, and we are asking for more cases. We would like to get the cases to NIH here. They are fully prepared to admit them. Now, I don't think an angiosarcoma case could recover."

Another question was asked - can alcohol stress reduce the induction period? Dr. Popper replied: "I don't know. Number one, we have to know first the metabolic pathway. The only ones who to my knowledge have done extensive biochemical studies, I mean metabolic studies, is Dr. Fahring from Dow Chemical Company. We are trying now, and again I am in a position here where I can try and persuade people to work. The pharmacology section in the Heart Institute is prepared to study the metabolism and I think that is a key question because until know the metabolism, you can't know whether alcohol aggravates or protects. It could well be that alcohol protects. Right now we are just philosophizing."

Dr. Maltoni [illegible] at this point: "I am glad you emphasized this point because [illegible] Dr. Wehrinberger and myself discussed this and we don't have any data about the metabolism, we don't have any data to confirm, there is no evidence [illegible]."

Dr. Rogers [illegible] said: "We know a little. Probably the chances are pretty high that [illegible] virus plays a role, and this is to me, for other reasons, extremely important. If it is so, then there may be a good chance to treat the [illegible] effectively in the liver. The hepatic [illegible] may be responsible for the appearance of [illegible] as in the liver. But, I have our [illegible] report as long as I am privileged to talk. The group in the Research Triangle may wish to look in animals for the precursor lesion, which is [illegible] important at the [illegible]. When we saw Dr. [illegible] Talbot at the Cancer Society meeting, something about a month ago, he had no slides. He said he would send them and I have not yet received them. I was trying to persuade the people at the Research Triangle to set up the experiment. But the experiments are expensive and not so easily done. Now I am told that the Industrial Biotest people got the lesions very quickly. So could we not get the earlier slides from Industrial Biotest Laboratories? I am talking for Dr. Thomas, the material should come here to NIH. I will be leaving in three months and I don't want to take it away to Mount Sinai."

Dr. Popper wondered whether they sacrifice animals or whether they wait until they die. Dr. Chirigos stated there were many to take care of the late [illegible]. Dr. Richardson indicated that as a pathologist for EPA, he can go out and visit the other pathologists and he indicated that he realized that the precursor lesions are important and would take this matter up upon his return to EPA.

Dr. Fleming indicated that he realized that we are primarily concerned with environmental contaminants and how to keep them away from the people. Dr. Popper has valid points which have also concerned a number of people at EPA, even though it does not seem to be one of EPA's functions. This has to do with the question of what happens when you know that you have a population who have been exposed. Let us say that EPA or the other agencies are able to stop further exposure. It seems that the regulatory agencies have a dual responsibility to go to HEW or other agencies that are concerned with surveillance to effect health surveillance of the individuals who were exposed and make known to them that these individuals will need frequent clinical exams. Dr. Fleming asked if there is anyone who is concerned with that part of the government's program.

Dr. Kraybill replied that Cancer Control at NCI would be the one to contact. Miss Mellow (from Cancer Control) indicated that they would appreciate knowing about incidences such as the ones mentioned.

Dr. Kraybill thanked Dr. Popper and Dr. McAllister for their excellent presentations.

The Interagency Collaborative Group on Environmental Carcinogenesis (Ninth Meeting) was adjourned, with all attendees agreeing that the presentations and participants were most helpful in providing a better understanding of the vinyl chloride exposure cancer problem.

H.F. Kraybill, Ph.D.
Chairman

I.C. Blackwood
Recording Secretary

May 17, 1974

Industrial BIO-TEST Laboratories, Inc.
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

(492) VC

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Summary of Mortality & Tumor Data Among Vinyl Chloride Mice
IBT Number 663-03222 (MCA)

| No. Mortalities with Neoplasms | Location of Tumors | | | |
|---|---|---|---|---|
| | Lung | Liver | Skin Metastasis → Lun | |
| 4 (1 Male, 3 Females) | 2(50%) | 2(50%) | 2(50%) | 2 |
| 6 (1 Male, 5 Females) | 3(50%) | 4(66.7%) | 2(33%) | 1 |
| 19 (4 Males, 15 Females) | 17(89.5%) | 17(89.5%) | 3(15.8%) | |

Attachment II had not been received at the time of the mailing of the minutes. When it is received, it will be distributed.

Industrial BIO-TEST Laboratories, Inc.
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NORTHBROOK, ILLINOIS 60062

Summary of Tumors in Vinyl Chloride Exposed Mice
IBT Bioassay [illegible] VCM-INA

| Group, Animal No., Sex | Histopathologic Findings | | | Date of Death |
|---|---|---|---|---|
| | Lung | Liver | Skin | |
| T-I | | | | |
| 1023 Male, | AA (s)* | HS (s)** | | |
| 1110 Female | AA (s), Metastatic Skin Tumor | | EC*** (para-aural) | 3-20-74 |
| 1119 Female | | HS (s) | | 3-24-74 |
| 1200 Female | Metastatic Skin Tumor | | EC & MC† (Femoral region) | 3-30-74 |
| T-II | | | | |
| 1347 Female | Metastatic Skin Tumor | | EC(Abdomen) | 3-5-74 |
| 1309 Female | | HS (s) | | 3-18-74 |
| 1889 Male | AA (s) | HS | | 3-25-74 |
| 1382 Female | | HS (s) | | 4-2-74 |
| 1350 Female | AA (s) | HS (s) | | 4-5-74 |
| 1299 Female | AA (s) | | EC & MC (Inguinal Region) | 4-9-74 |
| T-III | | | | |
| 1538 Female | AA (s) | HS (s) | | 3-6-74 |
| 1532 Female | AA (s) | | LSQ | 3-7-74 |
| 1562 Female | AA (s) | HS (s) | | 3-9-74 |
| 1598 Female | AA (s) | HS (s) | | |
| 1405 Male | AA (s) | HS (s) | | 2-25-74 |
| 1494 Male | AA (s) | HS (s) | | 3-22-74 |
| 1574 Female | AA (s) | HS (s) | | 3-22-74 |
| 1531 Female | | HS (s) | EC & MC (Femoral region) | 3-23-74 |
| 1588 Female | | HS (s) | | 3-25-74 |
| 1593 Female | AA (s) | HS (s) | | 3-30-74 |
| 1505 Female | AA (s) | HS (s) | | 4-3-74 |
| 1565 Female | AA (s) | HS (s) | | 4-3-74 |
| 1409 Male | AA (s) | HS (s) | | 4-5-74 |
| 1543 Female | AA (s) | HS (s) | | 4-5-74 |
| 1544 Female | AA (S) | HS | | 4-5-74 |
| 1546 Female | AA (s) | HS (s) | MC (Axillary region) | 4-5-74 |
| 1535 Female | AA (s) | HS (s) | | 4-7-74 |
| 1432 Male | AA (s) | | | 4-8-74 |
| 1477 Female | AA (s) Metastatic Skin Tumor? | HS (s) | EC (Para-Aural) MC (Abdomen) EC(Pelvic region) | 4-9-74 |

Key to Symbols

* Alveologenic Adenoma of Lung (AA)
** Hemangiosarcoma of Liver (HS)
*** Epidermoid Carcinoma of Skin (EC)
† Mammary Carcinoma of Skin (MC)
Ⓛ Lymphosarcoma of Thymus
S = multiple lesions

Cases of Angiosarcoma of Liver among
Vinyl Chloride Workers in the United States
as of April 17, 1974

| Case number | Company and plant location | Age at diagnosis, race, sex | Month and year of diagnosis | Month and year of death | Duration of industrial (work) exposure to VC |
|---|---|---|---|---|---|
| 1 | Goodrich | 52 WM | 4-64 | 4-64 | 19 |
| 2 | Louisville, Ky. | 43 WM | 8-67 | 1-68 | 17 |
| 3 | | 36 WM | 5-70 | 9-71 | 13 |
| 4 | | 49 WM | 3-73 | 3-73 | 16 |
| 5 | | 58 WM | 12-73 | 12-73 | 28 |
| 6 | | 45 WM | 2-74 | - | 11 |
| 7 | | 43 WM | 2-74 | - | 18 |
| 8 | Union Carbide Charleston, W. Va. | 45 WM | ? | 3-68 | 18 |
| [illegible] | Goodyear | 40 WM | 4-61 | 8-61 | 7 |
| [illegible] | Niagara, N.Y. | 54 WM | 5-68 | 5-68 | 17 |

h. Medical Surveillance

The following recommendations are directed primarily at medical screening to detect liver disease and/or hepatic tumor. They should be considered in the context of routine health screening for any general employee health problems, including non-hepatic health conditions potentially related to vinyl chloride monomer exposure. Routine health screening should include at time of initial employment the recording of past medical history and the performance both of a general physical examination and certain basic laboratory procedures (e.g., complete blood count, urinalysis, chest x-ray); provisions should also be made for routine periodic health followup examinations.

Employees covered by the following specific recommendations shall encompass all persons engaged in vinyl chloride monomer production and polymerization, including personnel peripherally involved such as in clerical and management assignments. The recommendations shall be applied both as a pre-employment requirement and as part of periodic health follow-up. Screening priority should be given to current employees with prolonged and close potential exposure to vinyl chloride monomer, whether in present or past work settings.

(i) At time of initial employment, or upon institution of screening, physical examination shall be performed with specific attention to detecting enlargement of liver or spleen by abdominal palpation.

(ii) At time of initial employment, or upon institution of screening and annually thereafter, a medical history check-list shall be completed by the employee. This list shall include questions concerning:

(a) alcohol intake
(b) past history of hepatitis
(c) past exposure to potential hepatotoxic agents, including drugs and chemicals.
(d) past history of blood transfusions
(e) past history of hospitalizations

Completed medical check-lists shall be reviewed by a physician and should be acted upon as medically indicated for each individual employee.

(iii) At time of initial employment, or upon institution of screening, a serum specimen shall be obtained for screening with respect to the following five bio-chemical determinations of liver function:

(a) total bilirubin
(b) alkaline phosphatase
(c) serum glutamic oxalacetic transaminase (SGOT)
(d) serum glutamic pyruvic transaminase (SGPT)
(e) gamma glutamyl transpeptidase (GGTP)

dditional tests that may optionally be considered for use in screening include lactic dehydrogenase (LDH), serum protein determinations, serum protein electrophoresis, and platelet count. Laboratory analyses shall be performed in laboratories accredited by the College of American Pathologists or licensed in accordance with the provisions of the Clinical Laboratories Improvement Act of 1967.

(iv) If results of laboratory screening are normal, screening shall be repeated on an annual basis. If the person being screened has been employed directly in vinyl chloride monomer production or polymerization for 10 years or longer, screening shall be repeated every 6 months.

(v) If one or more liver function tests are abnormal, serum testing shall be repeated as soon as possible, preferably within 2 to 4 weeks. If no abnormalities are present upon rescreening, testing should be repeated in 3 months.

(vi) If abnormalities persist on rescreening, the employee shall be removed from contact with vinyl chloride monomer operations and individualized medical workup shall be instituted. Suggested as initial steps in medical workup are a complete physical examination and various special procedures such as hepatitis B antigen determination and liver scanning.

If liver function abnormalities are determined to be unrelated to liver disease (e.g., elevated alkaline phosphatase in a young, physically active man or elevated bilirubin in Gilbert's syndrome) or to be transient (e.g., due to recent hepatitis or recent alcohol intake), the employee may be permitted to return to vinyl chloride-related employment, subject to individual medical evaluation.

(viii) In view of the preliminary results of animal toxicology studies, it is recommended that no woman who is pregnant or who expects to become pregnant should be employed directly in vinyl chloride monomer operations.

# ANGIOSARCOMA OF THE LIVER

## A NATIONWIDE CASE SURVEILLANCE REGISTRY

In response to the recent discovery that at least some cases of angiosarcoma of the liver may arise from exposure to vinyl chloride, the U.S. Public Health Service is developing a nationwide surveillance registry for such tumors. This registry will be maintained jointly by the National Institute for Occupational Safety and Health and the Bureau of Epidemiology, Center for Disease Control. Physicians who have patients with this diagnosis currently under their care, or who have encountered such cases in their practice over the past 10 years, are urged to contact the Center for Disease Control. Information is desired concerning all such cases, regardless of assumed etiology. Address all information to:

Center for Disease Control
Building 1, Room 520
Atlanta, Georgia 30333

Attention: Clark W. Heath, Jr., M.D.
Philip J. Landrigan, M.D.

Telephone: (404) 633-3311, Ext. 3961

# ANGIOSARCOMA OF THE HUMAN LIVER



by

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Similar terminology or synonyms or semantics used for the same tumor are to be found in the literature.

1. Hemangio-endothelial Sarcoma
2. Malignant vascular tumor of the liver
3. Kupffer Cell Sarcoma
4. Hemangioendothelioma
5. Hemangioblastoma
6. Endotheliobiastoma
7. Reticuloendothelioma (Purdy Stout)
8. Angioplastic Sarcoma
9. Primary Hepatic Sarcoma
10. Angioblastic Sarcoma
11. Endothelioma, grades - undifferentiated, well-differentiated, and anaplastic
12. Hemangiosarcoma
13. Malignant Hemangiosarcoma
14. Malignant Hemangioendothelioma
15. Metastasizing Hemangioma

Historically, there are many reasons for the above fence-sitting type of terminology.

In 1940, James Ewing reports in his textbook, *Neoplastic Disease,* "*I do not believe, therefore, that the existence of a true angiosarcoma arising from blood vessels of the liver has been satisfactorily demonstrated.*"

As late as 1948, Rupert A. Willis in his textbook on *Pathology of Tumors* states, "*We come now to a difficult question: Do truly neoplastic angiomatous growths occur? They are very*

*rare and most supposed examples are either multifocal hamartomas or vascular tumors of other kinds."*



Thorotrast and Angiosarcoma of the Human Liver

1925----Egas Moniz of France first demonstrated that a radioactive material in the form of colloidal Thorium dioxide could be used in cerebral vessel visualization.

1930----Heyden Products manufactured Thorotrast for wide distribution in Europe and the United States for use in vascular visualization-arteriography-hepatosplenography- and cerebral graphy.

1932----The Council of Pharmacy of the American Medical Association took a stand against its use.

1940----Thorotrast was still in use, although animal experimentation had demonstrated the formation of cancers and in the liver, angiosarcomas.

1947----Finally discontinued when the human cases of angiosarcomas were reported.

It was K.H. Bauer of Germany who compared the time of appearance of neoplasms after the injection of thorotrast, experimentally produced in animals, with their average life expectancy and the average span of life in man. He came to the conclusion that such tumors should appear between the 12th and the 18th year after the injection into the vascular system of man (textbook).

1947----MacMahan, H.E., Murphy, A.S., and Bates, M.I., Endothelial Cell sarcoma of the liver following thorotrast injection, Am J Path, 23, 585-611.
The first case of angiosarcoma from thorotrast was reported in the U.S. The latency period was 17 years.

1961----Nettleship, A. and Fink, W.J., Neoplasms of the liver following injection of thorotrast, Am J Clin Path, 35, 422-426.
This was the 8th reported case of angiosarcoma of the liver due to thorotrast. The latency period was 16 years.

1961----Suckow, E.G., Henegar, G.G., and Baserza, R., Tumors of the liver following administrations of thorotrast, Am J Path, 38, 663-677.
10 cases of angiosarcoma of the liver were reported due to thorotrast used intravascularly. The latency periods were 3 to 24 years, with the average being 15 years.

1965----Da Silva Horta, J, et al, Malignancy and other late effects following the administration of thorotrast, Lancet, 2, 201-205.
22 additional cases of angiosarcoma of the liver were reported in this article.

By this time, hundreds of cases of angiosarcoma of the liver have been produced from this radioactive substance. It was first claimed there was no danger because thorotrast was an alpha emitter. However, the standard dose of 75 ml ordinarily used gives a gamma radiation equivalent of 1.37 micrograms of radium. The half-life of thorium is 1.39 x 10 years, and the radioactivity of thorium dioxide rises after 5 years; the breakdown products are active and reach a peak after 15 years. With the Kupffer cells being a storage point in the liver, one can easily see the damaging effect of radiation.

Arsenic and Angiosarcoma of the Human Liver

More than any other element of metal carcinogenesis, arsenic remains one of the enigmas. It is commonly referred to as one of the implicating factors in human cancer formations. One group in Chicago claims it is a producer of angiosarcoma of the human liver. It is for this reason that a short literature review is made.

Complicating the interpretations of studies dealing with arsenic is the fact that no satisfactory animal models have been found.

1947----Neubauer, O., Arsenical cancers-a review, Brit J Cancer, 1, 192-251.

The author estimated the latency of arsenical cancer to be 18 - 20 years.

1953----Sommers, S.C. and McManus, R.G., Multiple arsenical cancers of the skin and internal organs, Cancer, 6, 347-359.

The estimated latency of arsenical cancer was 13 to 50 years.

1956----Roth, F., Zeit Krebforsch, 61, 287-319.

1957----Roth, F., Zeitschrift Krebs Forschung, Bd., 61(s), 468-503.B.

3 hemangioendothelial sarcomas of the liver were described from 27 autopsies in vintner. Latency in the German Vineyard workers was 12 to 17 years. Estimated intake of arsenic was 53.7 gms over a 12 year period.

1959----Roth, F., Zentrelblatt Alleg Pathol, 100, 529-530.

8 hemangiosarcomas of the liver were reported in a study from 82 autopsies. These were vineyard workers exposed to chronic arsenic intoxication in the form of oral ingestion via insecticides, sprays, and dust.

1968----Regelson, W., Kim, V., Ospina, J., and Holland, J.F., One case of hemangioendothelial sarcoma of liver from Chronic Arsenic Intoxication by Fowler's Solution, Cancer, 21, 514-521.

Latency period of 17 years plus 7. The amount of arsenic ingested was estimated to be about 50 grams.

An Environmental and Industrial Chemical Registry is needed to face our daily environmental chemical exposure. Most recently, another case of angiosarcoma has been reported with no history of thorium dioxide or arsenic. The case was from the New York Hospital, Cornell Medical Center, and was in a 46 year old white male.

1974----Sussman, E.B., Nydick, L., and Gray, G.F., One case report of hemangioendothelial sarcoma of liver, AMA Arch of Pathol, 97, 39-42.

In summary, we have histologically angiosarcomas from thorotrast, arsenic and vinyl chloride, which have the same morphological appearances.

Spontaneous Angiosarcomas of the Liver in Animals

Rats - In the rat, this is an unknown entity. Dr. K.C. Snell at the National Cancer Institute, in thousands of animals, has never seen this lesion. I have in my files records of over 10,000 rats with many different strains and have never seen this lesion.

Mice - In mice, angiosarcomas do spontaneously occur. This is in the Haired and Hairless strain H.R. mouse. Hemangioendotheliomas (angiosarcomas) were observed in 45 out of 251 in the control groups.

(Deringer, M.K., J of the Nat Cancer Inst, 12, 437-445, Oct 1951). As would be expected, when O-aminoazotoluene was subcutaneously inoculated, the incidence of angiosarcomas increased. (Ibid., 17, 533-539, 1956). Swiss Albino mice have a spontaneous 5% occurrence of angiosarcoma of the liver.

Experimental Angiosarcomas in Animals due to Thorotrast

1936----Capillary angiosarcomas were produced in mice by F. Selbie. Selbie, F., Experimental production of sarcoma with thorotrast, Lancet, 2, 847.

1938----Reticulosarcomas (angiosarcomas) of the liver were produced by intravenous injections. Onufrio, O., Su di un caso di reticulosarcoma experimentale do thorotrast, Folia Med, 24, 1245 (probably used a different species).

Arsenic Experimentation in Animals and Its Effect on Man

An excellent monograph on Arsenicals has been written by A. Furst and will be published in the future by the World Health Organization Working Group on the Evaluation of Carcinogenic Risks of Chemicals to Man.

Chemicals Which Produce Angiosarcomas of the Liver in Animals

Nitrosodimethylamine -(Magee, P.N., Barnes, J.M., Brit J Cancer, 10, 114, 1956) Orally administered the chemical to rats.

Herrold, K.M., J of the Nat Cancer Inst, 39, 1009, 1967. Subcutaneous administration to Syrian Hamsters. Otsuka, H. and Kuwahara, A., Gann, 62, 147-156, 1971. By oral administration and subcutaneous injection to DDD and BAL b/c strain mice.

Urethane - Deringer, M.K., J of the Nat Cancer Inst, 34, 841-847, 1965. Gave intraperitoneal injections to DBA/2eBDe strains of mice.

1,2-Dimethylhydrazine Dihydrochloride - Syrian Golden Hamsters were given, in water daily, 0.156 mg to the female and 0.161 mg to the male. Angiosarcomas occurred in 89% of the females and 82% in the males. The tumors were in the liver lung muscle, heart, and pancreas. No such tumor is seen in the control. (Toth, B., Cancer Res, 32, 2818-2827, 1972)

Ethylhydrazine hydrochloride - 0.0125% was given in drinking water and 38% vascular tumors were produced in Swiss Albino strain mice. (Toth, B., Scientific Proceedings, AAPB, San Francisco, Ca., 1974) N,Butyl-hydrazine HCL - only lung cancer. 1-carbamyl-2-phenylhydrazine - only lung cancer. Control incidence of angiosarcoma in the Swiss Albino mouse is 5%.

Methylhydrazine - (a rocket fuel component) Syrian Golden Hamsters received 0.01% in drinking water. Angiosarcoma of the liver (malignant histiocytoma, Kupffer cell sarcoma) was produced in 32% of the females and 54% of the males. Latency period was 70 and 78 weeks. No such tumor was seen in the controls. (Toth, B. and Shimizu, H., Cancer Res, 33, 2744-2753, 1973)

1-carbamyl-2-phenylhydrazine - A 0.25% solution in drinking water was given throughout the life span of Swiss mice. Angiosarcomas of the liver occurred in 8 out of 72, and in the controls, 4 out of 44. (Toth, B. and Shimizu, H., J of the Nat Cancer Inst, 52, 241-251, 1974)

Are Environmental Hazards in This Group?

Hydrazines are used in industry as a rocket propellant. Monomethylhydrazines are used as corrosive agents. Maleic hydrazide used as a herbicide is hydrolysed to hydrazines. 2-Hydroxyethylhydrazine is used to ripen pineapples and is sprayed on. Phenylhydrazine is used in medicine for polycythemia vera.

Nephroblastoma

Since Professor C. Maltoni mentioned the high incidence of nephroblastoma in rats treated with vinyl chloride, a brief statement is included for the Interagency Group and the Environmental Protection Agency Task Force.

Renal Adenocarcinoma in our population has shown a rapidly increasing incidence with age in both sexes. This is well-documented by the State of California, Alameda County, Department of Public Health, California Tumor Registry (1960-1969). A review on Cancer of the Kidney - Etiology, Epidemiology, and Pathology has been recently published by J.L. Bennington in Cancer Research, 32, 1017-1029, November 1973. In view of Dr. Maltoni's

experiments, should not the vinyl chloride workers and families be studied with this lesion in mind, as well as the liver?

Howard L. Richardson, M.D.

Medical Officer Pathologist
Pesticide Office Program
Environmental Protection Agency

April 17, 1974

# ADDENDUM TO "ANGIOSARCOMA OF THE HUMAN LIVER"



by

Howard L. Richardson, M.D.

## Thorotrast

1972----Thorotrast induced hepatoma, Smoron, C.L. and Battifora, H.A., Cancer, 30, 1252-1259. A case of thorotrast hepatoma is presented in a 60 year old female with a latency period of 28 years. This article is an excellent review and states that an increase has taken place in Japan and Scandinavian countries. No increase in American U.S. citizens.

1973----Thorotrast induced hepatoma presented as hyperthyroidism, Kiely, J.M., Titus, J.L., and Orvis, A.L., Cancer, 31, 1312-1314, 1973. Since 1947, approximately 115 additional cases of malignant tumors of the liver have been noted. It is estimated there are still 50,000 to 100,000 carriers of this radioactive contrast media. Ref: Minn Med, 53, 1137-1139, 1970. Primary liver sarcomas 22 years after the administration. This contrast media is still the best for visualization of the cerebral vessels and is used for this purpose. Benefit versus risk ratio.

## Arsenic and Human Cancer Formation

Tseng, W.P., et al, Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan, J Natl Cancer Institute, 40, 453--, 1968. The arsenic level in some drinking water is above 0.6 ppm. In areas of high concentration skin cancer are 21.4 per 1,000 of population. In areas of low concentration - 2.6 per 1,000 of population.

In view of the reported cases of human arsenic angiosarcomas, a review of the histopathological material present in the Taiwan pathological laboratories is warranted because of the following report in the literature:

Tien-Wu Lin, et al, Serum alpha-fetoglobulin and primary cancer of the liver in Taiwan, Cancer, 30, 435-443, 1972, From the Department of Surgery, National Taiwan University Hospital, Taipei, Taiwan, Republic of China (Taiwan also has a large vinyl chloride manufacturing plant). Primary cancer of the liver is as high as that of Africa and other Asian countries. 5.5% of all autopsies. 19.5% of all male cancer patients at the above hospital in the last 10 years. No histological classifications were given.

A Review of Malignant Hemangioendothelicmas in Infants and Children (Angiosarcoma)

1961----Kauffman, S., and Stout, A., Malignant hemangioendothelicma in infants and children, Cancer, 14, 1189--, 1961. Malignant vascular tumors are rare at all ages, but almost curiosities in children. 129 cases are recorded in the Laboratories of Columbia University College of Physicians and Surgeons, New York, New York, during the past 54 years. 9 cases were in children less than 16 years of age or 7%. In a review of the literature only 9 other acceptable cases could be located in the neck, jaw & mouth, arm, femur, gluteal muscle, and leg. The 9 cases of Kauffman and Stout were distributed as follows:

(1) Age 9, male, lymph node of the neck with metastasis to the lung.
(2) Age 8, female, scapula tumor.
(3) Age 14, male, right erestor spinal musc[illegible]
(4) Age 23 months, female, liver angiosarcom[illegible]
(5) Age 13, female, distal phalanx of the right toe.
(6) Age 12, male, scalp.
(7) Age 17, female, right upper eyelid.
(8) Age 15, male, middle right finger (fifth).
(9) Age 7, female, thigh.

1969----Blumenfeld, T., Flemming, I., and Johnson, W., Juvenile hemangioendothelioma of the liver: Report of a case and review of the literature, Cancer, 24, 853--, 1969. Prior to 1961, these authors had four cases that survived surgery and two cases after. It is not clear what their yearly distributions were in their review, but they are as follows:

(1) Case of hemangioendothelioma in a 2½ year old female. The solitary nodule was removed and the patient still survived.
(2) 4 cases of solitary nodules successfully removed in children 2½ months and above in age.
(3) 36 cases with multiple liver tumors - all died within 6 months.

1973----Hansen, R.C., et al, Cancer, 32, 136-141, 1973. Describes a case in a 7 month old female of mesenteric hemangioendothelioma with thrombocytopenia which received radiation therapy and had a resolution after 1000 rads.

Statistical Occurrence of Hepatoblastoma in Children from Autopsy

1971----El-Domeiri, A.A., Huvos, A.G., Goldsmith, H.S., and Foote, F.W., Jr., Primary malignant tumors of the liver, Cancer, 27, 7-11, 1971. This study represents a twenty year review at the Memorial Hospital, New York City, between 1947-1966.

(1) 137 primary malignant tumors of the liver cells.
(2) 23 found in children (16%) under the age of 14 years with the youngest one 8 months of age. All had been diagnosed by the pathologists as hepatocellular carcinoma of the adult or embryonal type.

Adenocarcinoma

Synonyms and related terms: alveolar carcinoma, clear cell adenocarcinoma, dark cell adenocarcinoma, granular cell carcinoma, Grawitz tumor, hypernephroid carcinoma, hypernephroma, papillary cystadenocarcinoma, parenchymal carcinoma.

Nephroblastoma

This was the term used by Professor Maltoni, and in view of the vinyl chloride problem, needs histopathological clarification at the earliest possible date.

Synonyms and related terms: adenomyosarcoma, adenosarcoma, alveolar carcinoma, blastoma tumor, blastoma mesoblastica polyvalentia, carcinosarcoma, chondrosarcoma, developmental tumor, dysembryoma, dysembryoplasia, embryoma, embryonal adenocarcinoma, embryonal adenomyosarcoma, embryonal adenosarcoma, embryonal carcinoma, embryonal mixed tumor, embryonal nephroma, embronal

sarcoma, embryonary nephroma, fibro-lipo-osteoadenome atypique, fibrosarcoma, hypernephroid sarcoma, leiomyoadenosarcoma, leiomyosarcoma, malignant embryoma, malignant leiomyoma, malignant nephroma, malignant teratoma, mesenchymal tumor, mesoblastic nephroma, mesoblastic sarcoma, mesothelioma, mixed teratoid tumor, myoblastic sarcoma, myochondroadenosarcoma, myochondrosarcoma, myofibrosarcoma, myoma sarcomatodes, myosarcoma striocellulare, nephrogenous dysembryoma, osteoblastoma, rhabdomyosarcoma, round cell sarcoma, sarcoma fusocellulare, sarcoma musculaire, spindle cell sarcoma, teratoma, unclassified embryonal tumor, Wilm's tumor.

In view of the above bewildering nomenclature, I have written to Professor Maltoni on behalf of the Environmental Protection Agency to bring representative slides to New York on May 8-11, 1974 for the National Academy of Sciences' vinyl chloride meeting. I have also requested slides and block for the National Cancer Institute's Small Animal Tumor Registry.

Carcinoma of the Kidney in a 15 Year Male

1973----Pratt-Thomas, H.R., Spicer, S.S., Upshur, J.K., and Greene, W.B., Cancer, 31, 719-725, 1973. Until 1934, renal cell carcinoma in children was controversial and in doubt. However, by 1973, we now have a total number of 59 cases reported in the English literature.

# EPA Environmental News

O'Neill (202) 755-0344

FOR IMMEDIATE RELEASE WEDNESDAY APRIL 24, 1974

## EPA BANS USE OF CERTAIN VINYL CHLORIDE PESTICIDES

Russell E. Train, Administrator of the Environmental Protection Agency, today suspended from further sale all pesticide aerosols containing vinyl chloride for use in the home, food handling establishments, hospitals, or in other enclosed areas. He also urged prompt Congressional action on the pending Toxic Substances Control Act.

EPA listed 28 products known to be affected by this decision.

Train also requested the immediate recall of all of these pesticides from retail shelves and distribution channels. EPA estimated that some 19,000 spray cans manufactured or distributed by 24 firms will be affected. A list of the products is attached.

Vinyl chloride, a gaseous chemical, is strongly suspected as the cause of a rare form of liver cancer diagnosed in 12 industrial workers engaged in the conversion of vinyl chloride to the plastic polyvinyl chloride.

Train said, "I am seeking the immediate nationwide cessation of the sale of these pesticides and the recall of existing stocks."

(more)

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"While the public health implications of exposure to vinyl chloride from short pesticide bursts are undetermined, the link between the gas and the cancer is suspected strongly enough to make it prudent public policy to ban further use of these products," Train stated.

The rare cancer, known as angiosarcoma of the liver, has been found in human beings and test animals exposed to vinyl chloride. Preliminary EPA tests and calculations show that a 30 second burst from an aerosol pesticide could produce levels similar to those used in animal experiments although over shorter periods of time.

Today's action was taken under a provision of the 1972 Federal pesticide law which permits the EPA Administrator to issue an emergency order banning the sale, distribution or use of products likely to result in unreasonable adverse effects on health or the environment.

Train noted that the Toxic Substances Control Act, pending before Congress, would give the Federal government authority to test and regulate the use of chemicals such as vinyl chloride before they are marketed to the general public. This legislation was proposed by the Administration in early 1971 and still awaits final Congressional action.

Train stated that the authority contained in the pending legislation would make it possible to identify potentially dangerous chemicals, such as vinyl chloride, prior to their being marketed and would provide effective means for either banning or limiting the use of toxic substances. Train urged early Congressional action on the legislation.

EPA earlier released the brand names of 20 products that contained the vinyl chloride gas. Additional brand names are disclosed in today's suspension action.

All of the manufacturers or distributors of pesticides containing vinyl chloride, including outdoor products not affected by the suspension, have indicated a willingness to recall their products voluntarily. "This is commendable but the time involved in insuring voluntary compliance would delay achieving the most rapid possible removal of these pesticides from the marketplace," Train said.

All manufacturers of pesticides containing vinyl chloride as a propellant have informed EPA of their immediate intention to substitute other chemicals. Several requests to amend registrations have already been received by EPA.

Notice of the suspension will appear shortly in the Federal Register.

# # #

INDOOR AEROSOL PESTICIDES AFFECTED BY TODAY'S SUSPENSION

| Product | Company |
|---|---|
| Brulin Bug Bomb | Brulin & Co. |
| Paracide with Sevin | Carson Chemicals, Inc. |
| Demert Raw Roach, Ant and Wasp Killer | Demert & Daugherty |
| Cobra International Roach, Ant and Wasp Killer | Cobra International [D] |
| Rexall Ant and Roach Killer | Rexall Drug Co. [D] |
| Walgreen Ant & Roach Killer | Walgreen Laboratories, Inc. [D] |
| Flea Killer for Dogs and Cats | Chase Products Co. |
| Barcolene Spray Disinfectant | The Barcolene Co. |
| Coop Dairy Insecticide for Milk Houses and Animals | Farmland Industries, Inc. |
| Excelcide 16-oz. Aerosol Bomb | The Huge Co. |
| Navy Brand Thrifty 50 | Navy Brand Mfg. Co. [D] |
| Mothrid Moth Proofer | Hysan Corp. |
| Mothrid Moth Proofer Cedar Scented or Activated Moth Proof Spray Cedarized | Liberty Products Co. [D] |
| Nokout 25 Aerosol Insecticide | Hysan Corp. |
| Strike - Wasp and Hornet | Albert Woods Wholesale [D] |
| Nokout 35 Insecticide | Hysan Corp. |
| Spritz Metered Air Sanitizer | Hysan Corp. |
| Anchor Flea, Lice and Tick Bomb | Philips-Roxane, Inc. |
| F-L-T Bomb | Bio-Centic Laboratories [D] |
| WAYNE Flea, Lice and Tick | Allied Mills, Inc. [D] |

| Product | Company |
|---|---|
| Rogers' Insecticide and Repellent | Jay Rodgers Co. |
| Total Release Insect Fogger | Spray-Chem Corp. |
| Crown "Total" Complete Release Insect Fogger | Crown Chemicals, Inc. [D] |
| Roberts' "Total" Complete Release Insect Fogger | Roberts Laboratories [D] |
| Chaperone Flea & Tick Killer | Sudbury Laboratory |
| Pyrethrin Insecticide Pressurized Dairy Insecticide | Woodbury Chemical Co. |
| COOP Pyrethrin Insecticide Pressurized Dairy Insectide | Farmland Industries, Inc. [D] |
| Mid-Am Brand Pyrethrin Insecticide Pressurized Dairy Insecticide | Mid-America Dairymen, Inc. [D] |

[D] -- Distributor of Product Listed Above

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Manufacturing Chemists Association

CHRONIC VAPOR INHALATION TOXICITY STUDY
WITH VINYL CHLORIDE

I. Outline of Investigation

| | | |
|---|---|---|
| A. | Type and Length*: | 12-month vapor inhalation in White Mice<br>12-month vapor inhalation in Albino Rats<br>12-month vapor inhalation in Hamsters |
| B. | Number of Animals: | 800 Mice<br>900 Rats<br>800 Hamsters |
| C. | Exposure Schedule: | Seven Hours per Day<br>Five Days per Week |
| D. | Test Materials: | Vinyl Chloride (Ethylene derived)<br>Total organic impurities less than 50 ppm |
| E. | Organization: | See Table I |
| F. | Dose Levels: | See Table I |

*After exposure, animals will be maintained for observation and sacrifice at end of two-year period (18 months for mice).

TABLE I

Chronic Vapor Inhalation Toxicity Study

Organization of Groups

| Test Material | | Group | Number of Animals | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Mice | | Rats | | Hamsters | |
| | | | Males | Females | Males | Females | Males | Females |
| None | | Control | 100 | 100 | 100 | 100 | 100 | 100 |
| Vinyl Chloride (Ethylene derived) | TE-I | Low level - 50 ppm | 100 | 100 | 100 | 100 | 100 | 100 |
| | TE-II | Intermediate level - 500 ppm | 100 | 100 | 100 | 100 | 100 | 100 |
| | TE-III | High level - 5000 ppm | 100 | 100 | 100 | 100 | 100 | 100 |
| | TE-IV | High level - 5000 ppm, with food, water, and cedar shaving bedding in cages during exposure | - | - | 100 | - | - | - |

Conditions in European study



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II. Chamber Parameters

Each group of animals will be exposed in a specially constructed stainless steel inhalation chamber having a capacity of approximately 9.2 $M^3$, allowing animal loading of less than 2% when the animals reach maturity. Flow rate through the chamber will be at least 0.92 $M^3$/min. providing a theoretical air change every ten minutes. The chamber supply air will be filtered and maintained at 40% to 60% relative humidity and 70° to 75°F.

III. Animal Parameters

A. Clinical Observations

All animals will be observed daily for lesions and behavioral changes attributable to the test material. The time of appearance and location of all tumors that occur among both control and test animals will be recorded. Mortality records will be kept on all groups of animals. All animals which die during the study will be necropsied and their tissues processed in accordance with the methods given in the Anatomic Pathology Section. Care will be exercised to minimize loss of tissues through cannibalism or autolysis. Animals in a moribund state will be sacrificed *in extremis* when death is imminent.

B. Body Weights

Individual body weights will be recorded once before exposure and after 1, 2, 3, and 4 weeks of testing. Thereafter, mean group body weights will be determined monthly up to the 12-month point of the study.

C. Clinical Pathology

Hemoglobin, hematocrit, total erythrocyte and total leukocyte counts will be performed at 18 and 24 months on 30 (15 male and 15 female) rats of the control and each test group. Differential leukocyte counts will be performed on all animals having high total leukocyte counts.

D. Anatomic Pathology

1. Methods of Sacrifice

Upon completion of the study, all survivors will be sacrificed by exsanguination following carbon dioxide anesthesia.

2. Gross Pathology

Complete necropsies will be performed on all animals which die or are sacrificed and all macroscopic lesions will be recorded. The lungs will be inflated with formalin fixative.

3. Histopathology

Representative specimens of the following organs

and tissues will be taken from all animals at time of sacrifice and fixed in 10.0% neutral buffered formalin:

Adrenal Glands
All Gross Lesions
Bone (femur, tarsal and metatarsal, including long bones of all four limbs)
Bone Marrow (sternal)
Brain
Both Ears (external auditory canal with ceruminal (Zymbal's) glands)
Esophagus
Eye
Gonads (testes and ovaries)
Kidneys
Large Intestine (caecum and colon)
Liver
Lungs
Lymph Nodes (tracheobronchial, cervical and mesenteric)
Optic Nerve
Pancreas
Parathyroid Gland
Pituitary Gland
Prostate
Salivary Gland
Seminal Vesicles
Skin
Small Intestine (duodenum, jejunum and ileum)
Spleen
Stomach
Thymus
Thyroid Gland
Tracheo
Urinary Bladder
Uterus

The above tissues, from animals of the control, TE-II, and TE-III will be processed by conventional methods, embedded in paraplast, sectioned (4-6$\mu$), stained with hematoxylin and eosin, and evaluated by light microscopy. If

drug-related lesions are detected in tissues from the high or intermediate dose (TE-II or TE-III) animals, affected tissues from the TE-I group animals will be processed and examined in the same manner as the above.

Only major organs (liver, kidney, spleen, heart, lungs) and neoplasms from animals which die and are found in an advanced state of autolysis will be processed for histopathologic evaluation.

Program in effect as of
July 13, 1973

Manufacturing Chemists Association

# EPIDEMIOLOGICAL STUDY OF MORTALITY IN VINYL CHLORIDE WORKERS

## Objectives

(1) To compare the mortality of individuals who have worked in vinyl chloride plants with that of the general population, corrected for area, age, and sex;

(2) to compare mortality patterns within the population of vinyl chloride workers, based upon estimated occupational exposure; and

(3) to compare mortality among vinyl chloride workers with the mortality of other occupational groups which TCA, Inc. has studied.

## Study Design

In each plant, the study population will consist of all workers who were employed for at least one year, beginning at the earliest date for which records are available, and ending on December 31, 1972. It has been estimated that this group will consist of approximately 5,000 current employees. Experience of the contractor indicates that retirements, terminations, and deaths before December 1972 will increase the total study population to about 7,500.

For each person, age, date of employment, nature and duration of employment, and ethnic origin (if possible) will be determined. For those who have died, copies of the death certificates will be obtained, either from plant records or from the public health authorities. These will be classified by cause of death, using the same rules as are used in national death statistics.

Those who left employment will be traced to establish their present status, using post office notification, drivers license records, and other methods which in the past have enabled tracing over 96 percent of our study population.

Data Analysis

Depending on the actual population size and the duration of follow-up activities, it appears probable that about 800 to 1,000 deaths will be covered in the study group.

The basic mortality analysis will begin with a calculation of the number of person years of observation contributed by the study group at each year of age and at each point in time during the study period, using a computer program prepared specifically for this purpose. These data will be used together with the observed deaths at each age and each point in time to calculate mortality rates, which will be compared with the mortality to be expected in the comparable U. S. population, as obtained from national statistics. Techniques of this kind are well developed and have been used for some time in chronic disease studies. (See California Tumor Registry, Cancer Registration and Survival in California, California State Department of Public Health, 1963.)

The above analysis will be repeated for specific causes of death, paying particular attention to competing risks, or interaction among different causes of death.

In addition, analysis of general and cause-specific mortality will be repeated for subgroups of the study population identified as having high, medium, and low exposure. The resulting mortality figures will be interpreted not only in light of their statistical significance, but for their relevance to known and suspected mechanisms of action of vinyl chloride, and for their implications with respect to future studies of special areas and groups.

The contractor has a data bank of mortality profiles, which provide a realistic standard against which to compare vinyl chloride workers, and which furnish a second bench mark in addition to the general population statistics.

Program in effect as of
July 13, 1973

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MANUFACTURING CHEMISTS ASSOCIATION

1825 CONNECTICUT AVENUE, N.W. WASHINGTON, D.C. 20009 (202) 483-0126

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HEALTH DOCKET-36

28 MAY 1974

The attached chronology concerns attention to occupational health aspects of vinyl chloride, particularly that in which the Manufacturing Chemists Association (MCA) has had a part on behalf of U. S. producers of vinyl chloride monomer (VCM) and polyvinyl chloride (PVC).

This material is provided as background and for use as you wish.

MANUFACTURING CHEMISTS ASSOCIATION
1825 CONNECTICUT AVENUE, N. W. WASHINGTON, D. C. 20009



FOR RELEASE

CONTACT:

For Immediate Release

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# VINYL CHLORIDE CHRONOLOGY

While it had been recognized for decades that exposure to high concentrations of vinyl chloride monomer (VCM) might cause liver and kidney injuries, the U. S. chemical industry was not aware of any cancer-related potential of VCM until May 1970.

From the time polyvinyl chloride (PVC) -- the principal product of VCM -- was first produced in this country in the 1930s, the major worker hazard concern with VCM was believed to be flammability and explosions. Controls were designed to cover these.

The Manufacturing Chemists Association's (MCA) Chemical Safety Data Sheet on vinyl chloride, published in 1954, stated, "Aside from the risk of fire or explosion, vinyl chloride presents no other very serious problem in general handling. The presently accepted maximum allowable concentration is 500 parts per million (recommended by the American Conference of Governmental Industrial Hygienists -- ACGIH -- later in 1962) . . . In concentrations well above 500 ppm, vinyl chloride acts as a mild general anesthetic."

(more)

In 1961, The Dow Chemical Company reported that long-term ($4\frac{1}{2}$ to 6 months at what would correspond to normal working hours) VCM exposures of animals to down to 100 ppm VCM resulted in slight liver injuries, and recommended working exposure levels be reduced to 50 ppm.

This recommendation for worker exposure was not accepted by ACGIH. In 1962, on the basis of work done at Yale University, from which the authors concluded that 500 ppm offered an adequate safety margin for human exposure to VCM, ACGIH published 500 ppm as the recommended standard.

In 1971, the Occupational Safety and Health Administration (OSHA) established 500 ppm VCM as a national standard. This changed in April 1974 when OSHA, following voluntary disclosure by The B. F. Goodrich Company of liver cancer deaths possibly related to vinyl chloride exposure, set a temporary emergency standard at 50 ppm. Then, on May 10, citing the findings of an MCA-administered study that showed liver cancer in mice at 50 ppm, OSHA proposed a "no detectable" standard, as previously recommended by the National Institute of Occupational Safety and Health (NIOSH).

The following is a brief chronology of vinyl chloride activities, relating to worker health. It is based on MCA records and input from U. S. producers of VCM and/or PVC.

(more)

January 1967 — Because of reports of finger abnormalities in the early 1960s, MCA arranged for a study at the University of Michigan on acroosteolysis -- softening of finger tip bones -- among VCM/PVC workers, particularly those who cleaned polymerization kettles. Study covered clinical, epidemiological and industrial hygiene aspects.

August 1968 — Research by The Dow Chemical Company showed slight alteration in liver function in workers industrially exposed to concentrations of up to 300 ppm VCM.

February 1970 — Findings of the MCA acroosteolysis study were submitted for scientific publication. They appeared in the "Archives of Environmental Health," published by the American Medical Association in January 1971. The authors were unable to pinpoint the cause of this disease and recommended animal studies be undertaken to develop an experimental model. They also recommended a worker exposure limit of 50 ppm VCM.

May 1970. — At the 10th International Cancer Congress, Houston, Texas, Dr. P. L. Viola, of the Regina Elena Institute for Cancer Research, Rome, Italy, reported 30,000 ppm VCM exposures at four-hours-a-day, five-days-a-week for a year, caused cancers of the skin, lung and bones of rats. He concluded that "no implications to human pathology can be extrapolated from the experimental model reported in this paper." He exposed these animals in an attempt to develop an experimental model for acroosteolysis.

August 1970 — ACGIH considered a reduction of the worker exposure limit to 200 ppm VCM, but did not publish it as a recommendation until August 1972.

(more)

September 11, 1970 — In spite of Dr. Viola's study and his conclusions of no human implications, MCA's long-standing Occupational Health Committee (OHC) considered the need for additional VCM research.

October 27, 1970 — At the suggestion of the OHC, MCA wrote to a number of laboratories regarding the conducting of toxicological studies on laboratory animals with VCM.

April 12, 1971 — MCA invited Dr. Viola to visit with the OHC and discuss his findings.

May 5-6, 1971 — Dr. Viola came and discussed his work to date and referred to other European studies in progress. He stated the vinyl chloride used in his tests was impure. He reported tentative observation of tumors in the ears of rats exposed to 5000 ppm VCM, but gave his opinion that 2500 ppm would not produce this effect. He stated that he would not be concerned about workers exposed to less than 500 ppm VCM.

May 6, 1971 — MCA's OHC recommended U. S. VCM/PVC producers sponsor animal exposure and epidemiological research on VCM carcinogenicity (cancer-causing) to be administered by MCA.

May 1971 — MCA acted on Dr. Viola's statement that other studies were being conducted in Europe and attempted, unsuccessfully, by correspondence and direct visits of a U. S. company representative, to learn of them.

July 7, 1971 — MCA corresponded with medical contacts of member companies, alerting them to potential occupational health problems with VCM and asked them about interest in supporting related research.

(more)

November 5, 1971 — MCA received a letter from Dr. Viola confirming observation of tumors in rats at 5000 ppm VCM (and perhaps less) and made some suggestions for further animal studies.

November 16, 1971 — At a vinyl chloride meeting arranged by MCA in Washington for interested U. S. company representatives, a European representative of Solvay et Cie. reported that he was aware of further studies just beginning in Europe. He said it was too soon to expect any data, and that he was not free to describe the source of his information nor the location of the studies. He said the exposure concentrations ranged from 20,000 ppm to 50 ppm and that groups of 25 male and 25 female rats were being exposed. He expressed concern about the purity of the vinyl chloride used in Dr. Viola's original study, since it was reported to contain one to three percent of impurities. The representative stated that Dr. Viola had observed a 10 to 15 percent incidence of ear tumors in rats exposed to 5000 ppm of vinyl chloride. Suggestions for epidemiological and animal exposure studies to be administered by MCA, on behalf of interested companies, were discussed at this meeting.

March 30, 1972 — Seventeen U. S. companies had agreed to financially support VCM studies.

April 1972 — MCA's Chemical Safety Data Sheet on vinyl chloride was revised to state: "Recent research studies reported from Italy indicate that repeated, long-term high level exposures of rats to vinyl chloride monomer vapor can result in the development of malignant tumors. However, many years of industrial experience with human exposures to concentrations frequently far above current standards have not demonstrated any carcinogenicity to humans."

(more)

April-June 1972

To enable the MCA program to be designed so as to yield data of optimum significance, overtures were made by MCA to establish technical liaison with the new European research mentioned at the November 16, 1971, meeting in Washington.

August 16, 1972

A letter to MCA bearing this date, sent on behalf of the European sponsors, offered technical cooperation under the condition that "no disclosure of information arising from the European investigation should be made outside the individuals comprising the technical coordinating task group without the specific consent of the European group." The purposes of such restriction were (1) that preliminary indications not be released until they had been validated, thereby to minimize unwarranted speculation, and (2) that releases remain subject to the control of the project's proprietors.

November 14, 1972

At an MCA meeting of company technical officials, an MCA representative who visited Europe October 19-20 reported he had obtained a copy of the testing protocol of Dr. Cesare Maltoni, director of the Institute of Oncology, Bologna, Italy, the principal investigator of the European sponsors, and was told only that results were surprising. The European group declined to release European data because agreement had not yet been reached to comply with the European group's stipulation of confidentiality.

December 1972

After much deliberation and with great reluctance to pledging confidentiality, the participating U. S. companies and MCA did so in an MCA communication to a representative of the European group. This was done because of the vital importance of learning of any indications from the European research, and thus having a base to proceed on further studies, if needed, without the delays which could have resulted from duplications of effort.

(more)

January 17, 1973 — The U. S. VCM/PVC industry technical delegation visited the European sponsors and Dr. Maltoni's facilities to learn in more detail about his experimental procedures and results.

January 30, 1973 — At an MCA meeting of participating company technical representatives, a brief oral progress report on Dr. Maltoni's work was presented by those who had visited him. It was reported that, in experiments with rats, in addition to tumors of the ear canal, tumors of the kidney and liver were observed at concentrations as low as 500 and 250 ppm VCM, but not at 50 ppm nor in the controls. The European work was observed to be of high quality, similar to that which would be done in U. S. laboratories. At this meeting, it was decided by the U. S. group of participating companies to initiate an epidemiological study of VCM/PVC workers, recognized earlier as an important complement to animal testing, but most usefully carried out with the benefit of the animal research background.

January 31, 1973 — MCA wrote to prospective contractors regarding an epidemiological survey.

February 1, 1973 — Having benefited from the European study indications in setting the protocol for the MCA research program, MCA signed a contract with Industrial BIO-TEST Laboratories, Inc., to conduct animal exposure studies. Subsequently, a press release was issued announcing, on behalf of participating companies, animal inhalation studies with VCM that would expose rats, mice and hamsters to VCM concentrations of 2500, 200 and 50 ppm for one year, with the animals to be kept on observation for an additional year. By contractual stipulation, the study results would be made public.

February 20, 1973 — Four prospective contractors met with MCA to discuss the epidemiological study.

(more)

March 1973 — MCA and participating companies initiated steps to present the details of VCM-related research to the appropriate U. S. government agency.

April 17, 1973 — MCA proposed to meet with executives of sponsoring companies of the European project concerning the desire to make a presentation to the U. S. government, with inclusion of European research observations, the latter preferably presented by a representative of the European group. A date of May 9 was suggested for this visit, but it proved impossible to arrange until mid-June.

June 15, 1973 — Following up on the proposal, four MCA representatives visited European group executives in Brussels. They were given assurance of the European companies' willingness to release their data -- although still incomplete -- to the U. S. government, and agreement to participate in its presentation. The European companies requested time to prepare the information for prior release to their respective governments, also. A presentation to the National Institute of Occupational Safety and Health (NIOSH) was planned for the week of July 16.

June 27, 1973 — An MCA press release announced an epidemiological survey, to be conducted by Tabershaw-Cooper Associates, Inc., to document the health experience of present and former employees who worked with VCM. Again, by contractual stipulation, the results would be made public.

June 28, 1973 — MCA requested a meeting with NIOSH to brief the agency on the status and background of VCM research.

(more)

July 11, 1973 — Three U. S. industry representatives reported to the MCA group the results of the Brussels visit on June 15. The European information then discussed included epidemiological data which indicated no increase in gross mortality from cancer and no increase in cancer morbidity or incidence of cancer among workers exposed to VCM.

July 17, 1973 — A presentation was made to NIOSH. A summary of the published toxicity data on vinyl chloride, along with a description of the industry and full details of the studies contracted under MCA administration were presented by MCA representatives, with expressed interest in taking advantage of any suggestions NIOSH might offer. A representative of the European group (a physician), reporting on the European studies, said that tumors had been observed in rats down to 250 ppm, but that an epidemiological survey had indicated no increase in gross mortality from cancer and no increase in cancer morbidity or incidence of cancer among workers exposed to VCM.

Summer-Fall 1973 — Companies involved in the Tabershaw-Cooper survey assembled their personnel records and death certificates of employees having had vinyl chloride exposure.

November 28, 1973 — A further progress report of Dr. Maltoni's studies was given to MCA by a European group representative. Results confirmed earlier observation of malignant tumors in rats at 10,000, 6000, 2500, 500 and 250 ppm VCM, but not at 50 ppm.

January 23, 1974 — The B. F. Goodrich Company announced that Kentucky health officials and NIOSH had been notified of the company's investigation of whether cancer deaths of three workers in PVC operations in its Louisville, Ky. plant were related to occupational causes.

(more)

January 29, 1974 — Goodrich reported, in a press release, that the death of another former employee had been tentatively identified as due to angiosarcoma of the liver.

February 1, 1974 — MCA proposed to the European group that they make arrangements for Dr. Maltoni to come to the OSHA hearings on vinyl chloride, February 15.

February 6, 1974 — MCA issued a press release announcing that it had stopped circulation of its Chemical Safety Data Sheet on vinyl chloride, because of the Goodrich reports -- now questioning the validity of the Data Sheet statement noting that carcinogenicity to humans had not been observed.

February 15, 1974 — Goodrich reported the death of a fifth employee due to liver angiosarcoma.

February 15, 1974 — MCA and Dr. Maltoni presented separate statements at OSHA hearings on vinyl chloride, giving background on work done to date.

February 21, 1974 — Union Carbide Corporation notified NIOSH of the death of a PVC worker from liver angiosarcoma.

March 1, 1974 — The Goodyear Tire & Rubber Company, in a press release, announced a vinyl chloride worker fatality resulting from angiosarcoma of the liver.

March 6, 1974 — Goodrich reported cases of liver angiosarcoma in two living employees.

(more)

March 22, 1974 — Goodyear, in another press release, announced two more worker fatalities from liver angiosarcoma.

April 9, 1974 — Industrial BIO-TEST Laboratories phoned MCA and reported that preliminary findings in the animal exposure study showed angiosarcoma was produced in mice at 50 ppm VCM

April 10, 1974 — MCA reported these preliminary findings to OSHA, NIOSH and the Environmental Protection Agency (EPA) by phone.

April 15, 1974 — MCA representatives and officials from OSHA, NIOSH and EPA met at Industrial BIO-TEST Laboratories, Inc., Northbrook, Ill., to be briefed on the findings.

April 16, 1974 — MCA issued a press release announcing preliminary indications that VCM exposure produced liver cancer in mice at several exposure levels, down to 50 ppm.

April 16, 1974 — Firestone Plastics Company, Division of The Firestone Tire & Rubber Company, in a press release, announced an angiosarcoma death of a PVC plant employee.

May 7, 1974 — In another press release, the results of the Tabershaw-Cooper survey were given. The survey showed that workers exposed to VCM have experienced overall death rates from cancer that are comparable to those experienced by other U. S. industrial populations, but less than in the general public. This is in spite of the now well-recognized risk of higher incidence of angiosarcoma of the liver among such workers. Also, there did appear to be suggestive dose-related increases in cancer incidence in respiratory tracts and the brain in longer-exposed workers.

(more)

May 10, 1974

It was reported at the New York Academy of Sciences' meeting that The National Cancer Institute had diagnosed a liver angiosarcoma in a living Union Carbide employee. The company reported this case to NIOSH in March 1974 as a liver ailment.

Four supplementary research projects on VCM proposed for MCA administration are now in near prospect:

- Rat metabolism study
- Rat fetus study
- Animal chronic exposure study at levels below 50 ppm VCM
- Animal acute exposure study to test potential effects from a possible single massive release causing extremely high VCM atmospheric concentrations.

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# Occupational carcinogenesis



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Occupational carcinogenesis is one of the most interesting, tragic, important and difficult fields in oncology.

It is interesting from the scientific point of view because it represents, dramatically, an experiment in carcinogenesis made on humans and it may teach us a lot about the natural history of tumours. It is tragic from a human point of view, because work which is per se a natural necessity of life, should not, at least, cause cancer. It is socially important because oncogenic factors increasingly are produced and diffused in occupational environments. Moreover from the factories they spread to the general environment, so that they come to be an ecological problem. Finally, occupational carcinogenesis is a difficult field to approach, because the care of the workers' health is often in conflict with the productive interests of the factories.

Industry has done a lot for experimental carcinogenesis, related to occupational cancer; often however the result is merely to prove the carcinogenic effect in animals of agents which have already proved to be carcinogenic for man: this is equivalent to saying that many people die of cancer but some make their living from cancer. On the other hand emotional arguments should be avoided. Thus I am aware that speaking on occupational carcinogenesis is a complex and difficult task.

Experimental carcinogenesis did not start with the experiment of Yamagiwa and Ichikawa in 1915, but rather in the 16th century with the observation of the so-called 'mountain disease' in miners of Joachimisthal. This disease was recognized at the end of the last century as pulmonary carcinoma, which we now know is due to radio-active pollution, present in those mines. In 1775 Percival Pott in 'Chirurgical Observations' described a cancer of the scrotum in chimney sweepers and he correlated it with the black soot. In 1894 Unna reported on the frequency of skin cancer found in maritime workers, and he considered it due to excessive exposure to sun light. In 1895 Rehn, a surgeon from Frankfurt, reported at the congress of the German Society of Surgeons, 3 cases of bladder tumours found among 45 workers from a factory which produced fuchsine. He thought that the tumours were caused by aniline, but in fact it was shown, several decades later, that they were due to other aromatic amines. In 1902 at a meeting of the Medical Society of Hamburg, Frieben presented a case of a cutaneous tumour found on the hand of an employee of a factory producing X-ray apparatus. This employee used his hand for radiological demonstrations.

The frequency of reports on occupational cancer has been increasing with the increase of industrialization, mainly due to the progress of chemistry. The most important thing to do in occupational carcinogenesis is to try to recognize occupations which may represent an oncogenic risk, and to identify the agent or agents which cause the risk, and also to try to assess the degree of risk. If the risk is related to an agent already known to be oncogenic for man, its detection in the occupational environment should be considered sufficient for undertaking preventive measures. On the other hand if the risk is related to agents, whose effects on workers have not yet been studied and are therefore not yet known, then we have to evaluate the risk they represent for workers. This can be done by means of epidemiological investigations and experimental testing. Most oncogenic occupational agents have been identified on the basis of retrospective epidemiological studies.

The progress in and the development of this branch of oncology should facilitate systematic experimental testing of agents heavily released in the occupational environ-

ment. In other words *epidemiological evidence in man should be avoided*. Experimental tests on animals are the more relevant to man, the more they reproduce the conditions of human exposure and eventually induce in animals the same tumours that they induce in man. In this case, the results of experimental tests may be considered largely equivalent to epidemiological evidence in man.

On the other hand if an agent causes any kind of tumour in animals, in whatever experimental conditions, it should be considered potentially carcinogenic for man. To consider an agent definitely carcinogenic for man on such a basis, would be an excess, but no time should be lost before retesting it in more appropriate conditions. To reproduce experimentally the conditions of occupational exposure is often difficult and costly. Furthermore we have to consider that the number of agents in the occupational environment is large and increasing.

Thus, new agents to which workers may be exposed should be submitted first to the easiest and quickest tests, however incomplete those tests may be. Then, for those agents inducing tumours in the experimental animals in these conditions, more precise and sophisticated experimental tests should be devised. The validity of experimental testing and the prerequisites for validity have been a matter of long discussions in international

**TABLE 1** *Incidence of subcutaneous sarcomas in rats, following local injection of some inorganic pigments*

| Treatment | No. of animals | No. of tumours |
|---|---|---|
| Chromium yellow (lead chromate) | 40 | 26 |
| Chromium orange (lead chromate) | 40 | 26 |
| Molybdenum orange (lead chromate and molybdenum chromate) | 40 | 36 |
| Cadmium yellow (cadmium sulphide) | 40 | 15 |
| Iron red (iron oxide) | 40 | 1 |
| Iron yellow (iron oxide) | 40 | 0 |
| Controls | 60 | 0 |

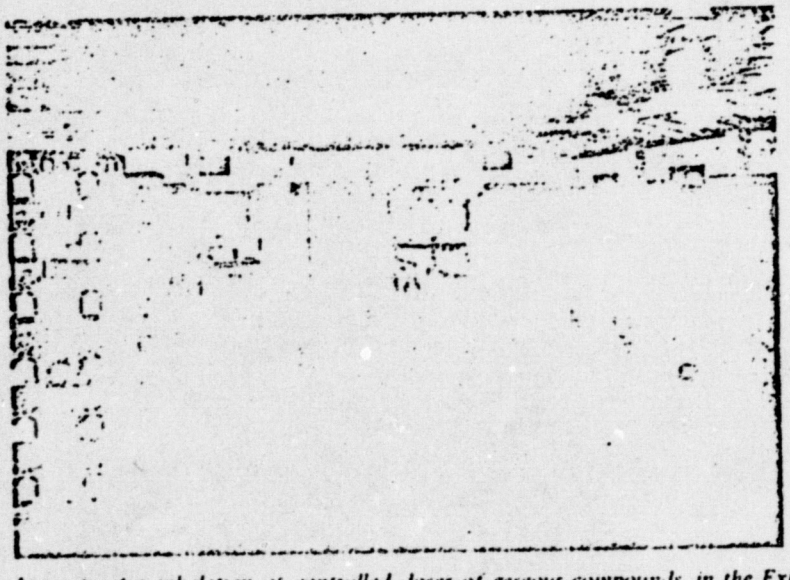


FIG. 1 *Apparatus for inhalation of controlled doses of gaseous compounds, in the Experimental Unit of the Istituto di Oncologia di Bologna.*

meetings and commissions, but of course, in the meantime the existing occupational exposure continues. Also, imperfect testing, for example the subcutaneous injection in the rat of compounds, to which man is exposed mainly by the respiratory route, may give some idea of their potential oncogenic risk.

In Table 1, data are reported on the induction of tumours (sarcomas) at the site of the subcutaneous injection of some inorganic pigments. From these data it clearly appears that chromium and cadmium pigments should be considered riskier than iron pigments. From what has been said before, the compounds shown to be carcinogenic in these conditions, should now be tested by inhalation. The latter way of exposure implies the availability of a complex apparatus for continuous inhalation of controlled doses. The apparatus is quite rare, as we discovered when we wanted to build one and we were not able to find any model in our own or any neighbouring country. Now an apparatus for inhalation of gaseous compounds has been functioning for more than two years in the experimental unit of our institute (Fig. 1).

With this apparatus we are now performing a carcinogenicity bioassay of vinyl chloride monomer (VC) and of vinyl acetate monomer (VA), which are (particularly the first) of great industrial importance. VC is used in the preparation of polyvinyl chloride resin, as a copolymer in saran and other plastics, as a solvent and as a chemical intermediate, and it is at present produced at a rate of 12,000,000 tons per year. Early results on these bioassays are shown in Table 2.

Zymbal glands carcinomas, liver angiosarcomas have never been observed as occurring spontaneously in our breed of Sprague-Dawley rats.

Only 3 cases of spontaneously occurring Zymbal glands carcinomas in rats (Sprague-Dawley) have been recorded in 1962. To our knowledge, no spontaneous nephroblastomas and liver angiosarcomas of rats have been reported in the literature. As far as we know, nephroblastomas have never been reported to be experimentally induced in rats; liver angiosarcomas have been induced in this species by diethylnitrosamine.

Although liver is the preferential site for onset of angiosarcomas, such kind of tumours have been observed in other tissues and organs: therefore VC should be considered in our experimental conditions generally cancerogenic for endothelia.

Zymbal glands tumours and nephroblastomas may be bilateral; liver angiosarcomas are often multiphocal.

Epidemiological investigations and medical controls should be undertaken on exposed workers. Would such neoplastic neoplasia unhappily be found in man, given the rarity of these tumours in both animals and humans, it would be a precise indication of the high value of experimental testing in predicting the oncogenic potential of environmental agents and would strengthen the recommendation on the necessity of such bioassays before any new industrial compound is produced and widespread in large scale.

Another means of revealing the oncogenic risk of an agent is to examine the exposed working populations with methods which make it possible to assess the incidence of cancer precursors. The incidence of such precursors has been studied by us by exfoliative cytology among asymptomatic, apparently healthy workers exposed to risk, namely among workers exposed to aromatic amines (urine cytology), and among workers exposed to chromates (sputum cytology). The incidence of cellular atypias in these two groups of workers is shown in Tables 3 and 4. It far exceeds the expected incidence.

To evaluate in medical and legal terms the risks represented by occupational oncogenic agents, we must consider that:

1. a direct relation exists between dose (amount and length of exposure) and neoplastic response;
2. the oncogenic agents produce mainly non-reversible changes, which may continue to develop when the exposure is interrupted;
3. the oncogenic agents (occupational or generally environmental) may be additive in their effects.

According to our knowledge the occupational carcinogenic agents may be classified as:

*(a)* definite carcinogens, when epidemiological evidence exists,

TABLE 2 *Preliminary results of carcinogenicity bioassay of vinyl chloride monomer (VC) and of vinyl acetate (VA) (From C. Maltoni, G. Lefemine and L. Gualano, in press)*

| Groups and treatment | Animals (Sprague-Dawley rats) | | Animals with tumours | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Zymbal glands carcinomas (A) | Nephroblastomas (B) | Angiosarcomas | | Other type and/or site | Total |
| | | | | | Liver (C) | Other sites | | |
| | Total | Survivors | No. | No. | No. | No. | No. | No. |
| I VA 2,500 ppm. | 96 | 15 | – | – | – | – | – | – |
| II VC 10,000 ppm. | 69 | – | 13 | 3 | 6 | – | 5 (H) | 27 |
| III VC 6,000 ppm. | 72 | 5 | 5 | 3 | 8 | 1 (D) | 1 (I) | 18 |
| IV VC 2,500 ppm. | 74 | 16 | 2 | 4 | 6 | 3 (E) | 1 (L) | 16 |
| V VC 500 ppm. | 67 | 15 | 2 | 3 | 5 | 2 (F) | 1 (M) | 13 |
| VI VC 250 ppm. | 67 | 20 | – | 3 | 1 | 2 (G) | 2 (N) | 8 |
| VII VC 50 ppm. | 64 | 35 | – | – | – | – | – | – |
| VIII No treatment | 68 | 33 | – | – | – | – | – | – |
| Total | 577 | 139 | 22 | 16 | 26 | 8 | 10 | 82 |

(A) Metastases to lung. (B) Metastases to liver and/or to lung and spleen. (C) Metastases to lung. (D) Angiosarcomas in subcutaneous fibrosing angioma. (E) 2 intrabdominal angiosarcomas (1 next to spleen and 1 next to ovary); 1 ossifying angiosarcoma of neck. (F) 1 pulmonary angiosarcoma; 1 angiosarcoma of uterus. (G) 1 intrabdominal angiosarcoma (next to spleen); 1 intrathoracic ossifying angiosarcoma. (H) 2 zymbal glands adenomas. 1 neurilemmoma of the ear; 1 mammary carcinoma; 1 cystoadenocarcinoma of ovary. (I) Sebaceous gland carcinoma of skin. (L) Zymbal glands adenoma. (M) Minimal deviation hepatoma. (N) 1 zymbal glands adenoma; 1 salivary glands carcinoma.

TABLE 3 *Frequency of cellular atypias among workers exposed to aromatic amines in 4 North Italian dye-stuff factories*

| Factory | No. of workers under control | Cytological classes (Papanicolaou) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | I | I-II | II | II-III | III | III-IV | IV | IV-V | V |
| A | 232 | 48 | 46 | 114 | 14 | 7 | 1 | 1 | – | 1 |
| B | 159 | 58 | 20 | 49 | 25 | 5 | 1 | 1 | – | – |
| C | 40 | 11 | 8 | 7 | 3 | 8 | 1 | 2 | – | – |
| D | 41 | 16 | 15 | 9 | 1 | – | – | – | – | – |
| Total | 472 | 133 | 89 | 179 | 43 | 20 | 3 | 4 | – | 1 |

TABLE 4 *Frequency of adenomatous typical and atypical hyperplasia, and of squamous metaplasia and dysplasia, in workers exposed to chromium compounds in one Northern Italian factory*

| Type of occupation | Length of exposure (years) | | Typical adenomatous hyperplasia | | Atypical adenomatous hyperplasia | | Squamous metaplasia | | Squamous dysplasia | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Length | No. | No. | % | No. | % | No. | % | No. | % |
| Production of chromates and dichromates | Up to 5 | 25 | 3 | 12 | – | – | 24 | 96 | 4 | 16 |
| | 6–10 | 14 | 3 | 21 | 1 | 7 | 12 | 86 | 3 | 21 |
| | 11–15 | 13 | 3 | 23 | 3 | 23 | 12 | 92 | 4 | 30 |
| | Over 15 | 17 | – | – | 1 | 6 | 15 | 88 | 4 | 23 |
| | Total | 69 | 9 | 13 | 5 | 7 | 63 | 91 | 15 | 22 |
| Production of chromium pigment | Up to 5 | 14 | 1 | 7 | – | – | 14 | 100 | – | – |
| | 6–10 | 17 | 1 | 6 | – | – | 14 | 82 | 2 | 12 |
| | 11–15 | 8 | 1 | 12 | – | – | 6 | 75 | 1 | 12 |
| | Over 15 | 8 | 2 | 25 | – | – | 8 | 100 | 2 | 25 |
| | Total | 47 | 5 | 10 | – | – | 42 | 89 | 5 | 10 |

*(b)* highly suspected carcinogens, when strong experimental and/or some epidemiological evidence is present,

*(c)* potential carcinogens, when experimental data give some indication of carcinogenic action of a compound on an experimental animal.

According to their effects, the carcinogenic agents may be classified as strong or medium.

The agents, which have been definitively proved or are suspected to be oncogenic for man on an epidemiological basis, are listed in Table 5, together with the target tissues and the degree of evidence. The list of the agents present in the occupational environment, which, on an experimental basis should be considered highly suspect or potentially carcinogenic for man, is reported in Table 6.

TABLE 5 *Agents proved or suspected to be oncogenic for workers on an epidemiological basis*

| Agents | Evidence | Tumours |
|---|---|---|
| U.V. radiations | + | Skin carcinomas |
| X-rays | + | Skin carcinomas<br>Leukaemias |
| Uranium ore | + | Pulmonary carcinomas |
| Arsenic | (+) | Skin carcinomas<br>(lung carcinomas) |
| Asbestos | + | Lung carcinomas<br>Pleural mesotheliomas<br>(abdominal malignancies) |
| Chromium | + | Lung carcinomas |
| Nickel | + | Lung carcinomas<br>Carcinomas of nasal and paranasal cavities |
| Iron ore | (+) | Lung carcinomas |
| Bis-chloromethyl ether | + | Lung carcinomas |
| Benzene | + | Leukaemias |
| Isopropylic oil | (+) | Carcinomas of paranasal cavities |
| Soot, tars, mineral oils, cutting oils | + | Skin carcinomas |
| Carbon black | + | Lung carcinomas |
| Mustard gas | + | Laryngeal carcinomas |
| Aromatic amines | + | Bladder and upper urinary tract carcinomas |

TABLE 6 *Agents suspected to be carcinogenic for workers on an experimental basis*

| | |
|---|---|
| Beryllium | Pesticides (DDT, aldrin, dieldrin, Aramite, DMDT, Amizol, Thiuram) |
| Cadmium | Thiourea and related compounds |
| Cobalt | Tannins |
| Lead | Detergents |
| Selenium | Alkylating agents |
| Zinc | Nitrosamines |
| Carbon tetrachloride | Azo-dyes |
| Chloroform | Oestrogens |
| Vinyl chloride | |

In Italy carcinogenic occupational risk exists for workers who are:

*(a)* exposed to chromates, mainly the ones working in factories where chromates are produced;

*(b)* exposed to nickel, mainly the ones exposed to nickel-carbonyl;

*(c)* exposed to asbestos, mainly the ones who extract it from its natural source, or workers in factories where asbestos is used for manufacturing;

*(d)* in factories making shoes, purses and raincoats, exposed to benzene;

*(e)* in factories producing carbon black from mineral oils; and

*(f)* in the dye and rubber industries, exposed to aromatic amines.

In our country occupational tumours have been observed in many of the above mentioned workers. 21 lung carcinomas have been found among less than 200 workers in a chromate factory in Northern Italy. Pleural mesotheliomas have been discovered among workers in asbestos mines. A number of leukaemias have been found among shoe-makers, who were heavily exposed to benzene, in factories in Lombardy (Vigevano), Bologna Province and Tuscany. The incidence of bladder and other urinary tract carcinomas among workers in 5 Italian dye-stuff factories are shown in Table 7. In these factories workers had been exposed to β-naphthylamine, benzidine, α-naphthylamine, Auramine, fuchsine, 3,3′-dichlorobenzidine. Now in our country the production of β-naphthylamine and benzidine has been withdrawn. One may conclude that prevention of occupational carcinogenesis is a very urgent problem.

The methods of prevention may be summarized as follows:

1. correct experimental testing of all newly used agents;
2. up to date epidemiological data from various categories of workers exposed to risk;
3. legislative measures forbidding the production and the utilization of agents which have been shown to be oncogenic on an epidemiological and/or an experimental basis, especially if the said agents are strong carcinogens;
4. measures of technical protection, when weak or doubtful carcinogens continue to be produced or employed; these protective measures should be periodically examined by Public Health inspectors;
5. specific medical checks to make possible, on the one hand, the early detection of preneoplastic lesions and tumours, and on the other, the quantitative evaluation of the risks through the incidence of these changes.

It is my opinion that the value of medical checks is mainly to evaluate the risk that is epidemiological. Early detection of occupational tumours which, as already shown, are mainly located in the respiratory and urinary tract, has been, I think, over-emphasized. We know that these tumours are multicentric. In other words all the target apparatus is in some way affected by the carcinogenic process.

TABLE 7 *Frequency of carcinomas of the urinary tract among workers of 5 Italian dye-stuff factories exposed to aromatic amines*

| Factory | Total No. of exposed workers | No. of workers with carcinoma | | |
|---|---|---|---|---|
| | | Bladder | Renal pelves and ureters | Total |
| A | 286 | 17 | 1 | 18 |
| B | 386 | 87 | 5 | 92* |
| C | 213 | 44 | – | 44 |
| D | 135 | 4 | – | 4 |
| E | 135 | 7 | 1 | 8 |
| Total | 1,155 | 159 | 7 | 166 |

* In 1 case bladder and upper urinary tract tumours were coexistent.

Concerning the urinary tract, in a systematic histological study, I have seen that in patients with bladder tumours, dysplastic and cancerous foci may be detected from renal pelvis to urethra. Therefore it is obvious that in such conditions early diagnosis can achieve very little. We may diagnose some tumours quite early, but on the basis of 15 years' experience with periodic checks of workers exposed to high risk, I doubt that periodical medical examination has a real bearing in saving people with occupational cancer although detected early, or in prolonging their life span. Thus my position is in sharp contrast with those who claim to 'protect' (!) workers exposed to carcinogenic risk with medical examinations. *I do believe that the potentialities of medical examinations should be evaluated at an international level.*

In conclusion, I would like to emphasize the need of a close collaboration among scientists, public health services, workers unions and industries, to evaluate the risks and to devise preventive measures for avoiding or minimizing occupational tumours.

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RENDICONTI DELLA CLASSE
DI SCIENZE FISICHE, MATEMATICHE E NATURALI

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CESARE MALTONI e GIUSEPPE LEFEMINE

# Le potenzialità dei saggi sperimentali nella predizione dei rischi oncogeni ambientali. Un esempio: il cloruro di vinile

Estratto dal fasc. 3, Serie VIII, vol. LVI – Marzo 1974

ROMA
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Serie VIII, vol. LVI, fasc. 3 - Marzo 1974

**Oncologia.** — *Le potenzialità dei saggi sperimentali nella predizione dei rischi oncogeni ambientali. Un esempio: il cloruro di vinile.* Nota di CESARE MALTONI e GIUSEPPE LEFEMINE, presentata (*) dal Socio G. FAVILLI.

SUMMARY. — A wide project of correlated and integrated experiments, performed for testing the carcinogenic potentialities of vinyl chloride (VC) (a monomer of high industrial importance), is presented.

The results showed that VC induces Zymbal's gland carcinomas, nephroblastomas, and hepatic and extra-hepatic angiosarcomas, in rats. and pulmonary tumours, mammary carcinomas and liver angiosarcomas, in mice.

The experimental data have oriented the clinical observations and the epidemiological investigations, which have recently brought to the detection of the early cases of liver angiosarcomas among exposed workers in the U.S.A. and in the U.K.

The experimental carcinogenicity bio-assays of VC should be considered therefore highly predictive. They represent a convincing example for potentiating experimental testing for all new industrial compounds, and for the ones already widespread, but on whose biological effects we are still ignorant.

In queste ultime decadi il numero e la quantità di agenti oncogeni prodotti e diffusi nell'ambiente di lavoro sono aumentati e vanno aumentando in maniera preoccupante. Dalle fabbriche gli agenti oncogeni vengono immessi nell'ambiente generale diventando in tal modo un problema ecologico.

Quale conseguenza di questa situazione viene registrato un aumento dei tumori professionali e da agenti esogeni ambientali in senso lato.

La maggior parte degli agenti oncogeni presenti nell'ambiente dell'uomo sono stati identificati sulla base di studi epidemiologici retrospettici.

*La prova epidemiologica dovrebbe essere evitata. Andrebbero invece eseguiti per tutti gli agenti di nuova produzione ed uso sistematici saggi sperimentali per predire le loro eventuali potenzialità oncogene.*

Tali saggi non vengono tuttavia eseguiti in genere in maniera sistematica, essenzialmente per due ragioni. La prima consiste nella mancanza di una normativa. La seconda nel fatto che, poiché spesso il disegno e la conduzione degli esperimenti non sono adeguati e pertanto le loro risultanze non estrapolabili all'uomo, attorno ad essi si è creato un certo scetticismo.

A nostro avviso invece il saggio sperimentale, se correttamente impostato e attuato, ha un alto valore predittivo.

Ne è un esempio quello che qui vi riferiamo. A nostro conoscenza è la prima volta che mediante un saggio sperimentale viene previsto con assoluta precisione il rischio oncogeno, l'entità del rischio e i substrati bersaglio.

(*) Nella seduta del 9 marzo 1974.

Le presenti indagini si riferiscono a saggi di cancerogenicità del cloruro di vinile (CV).

Questo monomero è di grande importanza industriale. Esso è usato nella produzione di cloruro di polivinile (CPV), come copolimero nella produzione di saran e di altre plastiche, come solvente e come intermedio chimico. Per un breve periodo è stato impiegato anche in anestesiologia. Il CV è prodotto nella quantità di circa 12.000.000 di tonnellate all'anno.

Vanno incontro a rischio di essere esposti a questo prodotto:

1) gli operai addetti alla produzione di CPV e di altre resine di cui è costituente, alla produzione di CV e alla utilizzazione industriale di CV per altri scopi;

2) gli operai che utilizzano il CPV;

3) gli abitanti di zone circostanti le fabbriche in cui viene prodotto CV e CPV; e

4) se pure in misura minore, coloro che utilizzano o vengono a contatto con plastiche a base di CV o con materiali in esse contenuti.

Il progetto di saggiare il potenziale oncogeno del CV fece seguito ai risultati preliminari del lavoro pionieristico del prof. Viola, presentato al X Congresso Internazionale sul Cancro (Houston, 1970) e che fu in seguito pubblicato su «Cancer Research» nel 1971 (Viola *e coll.*, 1971).

I risultati del prof. Viola indicavano che l'esposizione a 30.000 ppm di CV, 4 ore al giorno, 5 giorni la settimana, per 10 mesi, produceva tumori nel ratto. Nell'interpretazione del prof. Viola questi tumori originavano dalla cute, dal polmone e dalle ossa.

Immediatamente dopo il resoconto di Houston entrammo in contatto con il prof. Viola, che gentilmente mise a nostra disposizione le sezioni istologiche dei suoi tumori e il suo resoconto in extenso, ancora in pubblicazione.

Sulla base di questo materiale noi raggiungemmo le seguenti conclusioni:

1) nelle condizioni sperimentali del prof. Viola il CV mostrava chiaramente un effetto cancerogeno sul ratto;

2) 30.000 ppm di CV erano una dose estremamente alta;

3) i tumori descritti come cutanei originavano dalle ghiandole di Zymbal, che sono sensibili ad un largo spettro di agenti cancerogeni (2-acetilaminofluorene, benzidina, idrocarburi policiclici, aminostilbene, uretano, ecc.);

4) i tumori descritti come polmonari erano in realtà metastasi da carcinomi delle ghiandole di Zymbal; le localizzazioni neoplastiche polmonari erano osservate tutte in animali portatori di tumori delle ghiandole di Zymbal ed erano in tutto e per tutto simili a questi tumori.

Si impose pertanto l'urgenza di ricerche sistematiche per chiarire ulteriormente il tipo e il grado di effetto cancerogeno del CV con particolare riguardo a quei fattori sperimentali, correlati con l'esposizione, quali la via di somministrazione, la concentrazione, la durata, ecc., che possono dare più dirette indicazioni circa il rischio delle condizioni dell'ambiente professionale.

A questo proposito poiché l'Istituto di Oncologia ed il Centro Tumori di Bologna sono particolarmente specializzati in studi di prevenzione e controllo dei tumori, la Montedison, la maggiore produttrice italiana di CV, si è orientata a potenziare il nostro programma di saggi sugli effetti biologici del CV. Alla Montedison si sono in seguito unite la ICI (Gran Bretagna), la Solvay (Belgio) e la Rhone-Progil (Francia) (Gruppo Cooperativo Europeo per lo Studio degli Effetti Biologici del CV).

Prima di iniziare la fase operativa di questa ricerca è stato necessario preparare condizioni idonee per l'esposizione per via inalatoria.

Lo studio e la costruzione di un apparato per esposizione programmata e controllata ha richiesto alcuni mesi. Il controllo viene eseguito mediante gas-cromatografia. Un tale apparato rende possibile l'esposizione a concentrazioni variabili da 30.000 ppm a 50 ppm, e il trattamento simultaneo di 1200 roditori da esperimento. Essenzialmente l'apparato è costituito di acciaio inossidabile e cristallo.

Il CV è stato fornito dalla Montedison. Ciascuna fornitura è stata analizzata prima dell'uso per determinare le eventuali impurità: il CV da noi usato conteneva impurità di ordine trascurabile.

Gli esperimenti sono stati condotti principalmente su ratti del ceppo Sprague-Dawley; sono pure stati usati ratti Wistar, topi Swiss e criceti. Tutti gli animali eccetto i criceti sono stati allevati nel nostro Istituto per anni e qualunque sia stato il loro uso essi sono stati sottoposti a completa autopsia, per cui noi conosciamo la loro patologia spontanea corrente.

Sono stati iniziati in sequenza 14 esperimenti. Alcuni di essi sono stati programmati fin dall'inizio, altri invece sono stati ritenuti necessari in seguito, sulla base dei primi risultati sperimentali.

Il piano degli esperimenti alla data attuale è presentato nella Tabella I.

Essenzialmente abbiamo voluto verificare l'azione oncogena del CV, in relazione a vari fattori: vie di somministrazione, dosi, durata e ritmo dei trattamenti, specie a ceppo animale, ed età degli animali.

Inoltre abbiamo voluto saggiare l'eventuale possibilità d'azione trasplacentare del composto.

Tutti gli animali sono tenuti sotto osservazione fino a morte spontanea. Alla morte su ciascun animale viene eseguita una autopsia completa. Sono esaminati istologicamente di regola: le ghiandole di Zymbal, il grasso interscapolare, le ghiandole salivari, la lingua, i polmoni, il fegato, i reni, la milza, lo stomaco, diversi segmenti dell'intestino, la vescica, l'encefalo, le ossa delle zampe e ogni altro tessuto con lesioni patologiche. Tutti gli animali esposti alle dosi più alte (30.000 e 10.000 ppm) con o senza tumori vengono esaminati radiologicamente durante il trattamento e/o alla morte, per verificare l'insorgenza di eventuali lesioni acrosteolitiche.

Sono stati esaminati radiologicamente anche gli animali esposti a dosi più basse, quando portatori di tumori.

TABELLA

*Piano degli esperimenti*

| N. DEGLI ESPERIMENTI | TRATTAMENTO | | |
|---|---|---|---|
| | Via | Dosi di CV | Durata |
| BT1 | Inalazione | 10.000, 6.000, 2.500, 500, 250, 50 ppm. Controlli non trattati. Controlli trattati con 2.500 ppm di acetato di vinile (AV) | 4h/d/ 5d/sett/ 52 sett. |
| BT2 | Inalazione | 200, 150, 100 ppm. Controlli non trattati. | 4h/d/ 5d/sett./ 52 sett. |
| BT3 | Inalazione | 10.000, 6.000, 2.500, 500, 250, 50 ppm. Controlli non trattati. | 4h/d/ 5d/sett./ 17 sett. |
| BT4 | Inalazione | 10.000, 6.000, 2.500, 500, 250, 50 ppm. Controlli non trattati | 4h/d/ 5d/sett./ 30 sett. |
| BT5 | Transplacentale | 10.000, 6.000 ppm. | 4h/d/ 7d/ (dal 12° al 18°d di gravidanza) |
| BT6 | Inalazione | 30.000 ppm. | 4h/d/ 5d/sett./ 43 sett. |
| BT7 | Inalazione | 10.000, 6.000, 2.500, 500, 250, 50 ppm. Controlli non trattati. | 4h/d/ 5d/sett./ 52 sett. |
| BT8 | Inalazione | 10.000, 6.000, 2.500, 500, 250, 50 ppm. Controlli non trattati | 4h/d/ 5d/sett./ 30 sett. |
| BT9 | Inalazione | 50 ppm. Controlli non trattati. | 4h/d/ 5d/sett./ 52 sett. |
| BT10 | Inalazione | 10.000, 6.000 ppm. Controlli non trattati. | 4h/d/ 5d/sett./ 5 sett.; 4h/d/ 1d/sett./ 25 sett.; 1h/d/ 4d/sett./ 25 sett.; |
| BT11 | Ingestione | 16,6 mg; 3,32 mg; 50 mg/kg peso corporeo in olio di oliva. Controlli: olio di oliva | 1/d/ 5d/sett./ 52 sett. |
| BT12 | Iniezione intraperitoneale | 4,25 mg in 1,0 cc di olio di oliva. Controlli: 1,0 cc di olio di oliva. | 4, 3, 2 volte ogni due mesi e 1 volta |
| BT13 | Iniezione sottocutanea | 4,25 mg in 1,0 cc di olio di oliva. Controlli: 1,0 cc di olio di oliva. | 1 iniezione |
| BT14 | Inalazione | 10.000, 6.000 ppm. | 4h/d/ 5d/sett./ 5 sett. |

I

*all'1° marzo 1974*

| ANIMALI | | | | | | | DURATA DEGLI ESPERIMENTI ALLA DATA PRESENTE (in settimane) |
|---|---|---|---|---|---|---|---|
| Specie | Ceppo | Età (settimane) | N. ♀ | N. ♂ | N. Totale | N. Per gruppo | |
| Ratto | Sprague-Dawley | 13 | 268 | 309 | 577 | 64-96 | 130 |
| Ratto | Sprague-Dawley | 13 | 280 | 265 | 545 | 65-120 | 34 |
| Ratto | Sprague-Dawley | 21 | 262 | 288 | 550 | 60-190 | 59 |
| Topo | Swiss | 11 | 250 | 260 | 510 | 60-150 | 34 |
| Ratto | Sprague-Dawley | 19 (fattrici) Embrioni di 12 giorni | 110 | 36 | 146 | 30-54 | 68 |
| Ratto | Sprague-Dawley | 17 | 30 | 30 | 60 | 60 | 34 |
| Ratto | Wistar | 11 | — | 220 | 220 | 30-40 | 34 |
| Criceto | Dorato | 11 | — | 268 | 268 | 32-70 | 21 |
| Ratto | Sprague-Dawley | 11 | 200 | 200 | 400 | 300 (t) 100 (c) | 6 |
| Ratto | Sprague-Dawley | 11 | 420 | 420 | 840 | 120 | 6 |
| Ratto | Sprague-Dawley | 13 | 160 | 160 | 320 | 80 | 6 |
| Ratto | Sprague-Dawley | 13 | 150 | 150 | 300 | 60 | 6 |
| Ratto | Sprague-Dawley | 21 | 80 | 70 | 150 | 75 | 6 |
| Ratto | Sprague-Dawley | Neonati | — | — | 89 | 43-46 | 2 |

Nelle Tabelle II–VI vengono esposti i dati preliminari relativi agli esperimenti BT 1, BT 3, BT 6, BT 5, BT 4. Per quanto concerne gli altri esperimenti dobbiamo attendere ancora per avere risultati.

Da quanto presentato nelle Tabelle e dallo studio istologico emergono i seguenti punti:

1) il CV è oncogeno nelle condizioni sperimentali da noi saggiate: esso provoca carcinomi delle ghiandole di Zymbal (fig. 1), nefroblastomi (fig. 2) e angiosarcomi epatici (figg. 3, 4) e di altri tessuti ed organi (figg. 5, 6) nel ratto, e adenomi–adenocarcinomi polmonari, carcinomi mammarii e angiosarcomi epatici nel topo;

TABELLA II

*Esperimento* BT1: *Risultati sperimentali a 130 settimane*

| Gruppi e trattamenti | Animali (ratti Sprague-Dawley) | | Animali con tumori | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Totale | Sopravvissuti | Carcinomi delle ghiandole di Zymbal (A) | Nefroblastomi (B) | Angiosarcomi: Fegato (C) | Angiosarcomi: Altre localizzazioni | Altri tipi e/o localizzazioni | Totale (O) |
| | N. | | N. | N. | N. | N. | N. | N. |
| I) AV 2.500 ppm | 96 | — | — | — | — | — | — | — |
| II) CV 10.000 ppm | 69 | — | 16 | 4 | 7 | — | 6 (H) | 25 |
| III) CV 6.000 ppm | 72 | — | 7 | 4 | 13 | 2 (D) | 1 (I) | 24 |
| IV) CV 2.500 ppm | 74 | — | 2 | 6 | 14 | 3 (E) | 1 (L) | 24 |
| V) CV 500 ppm | 67 | — | 3 | 4 | 7 | 2 (F) | 1 (M) | 16 |
| VI) CV 250 ppm | 67 | 1 | — | 6 | 4 | 2 (G) | 2 (N) | 12 |
| VII) CV 50 ppm | 64 | 3 | — | — | — | — | — | — |
| VIII) Nessun trattamento . . . | 68 | 1 | — | — | — | — | — | — |
| TOTALE . . . | 577 | 5 | 28 | 24 | 45 | 9 | 11 | 101 |

A) Metastasi al polmone. B) Metastasi al fegato e/o al polmone e alla milza. C) Metastasi al polmone. D) 1 angiosarcoma in angioma fibrosante sottocutaneo; 1 angiosarcoma ossificante auricolare. E) 2 angiosarcomi intraddominali (1 vicino alla milza, 1 vicino all'ovaio); 1 angiosarcoma ossificante laterocervicale. F) 1 angiosarcoma polmonare; 1 angiosarcoma dell'utero. G) 1 angiosarcoma intraddominale (vicino alla milza); 1 angiosarcoma ossificante intratoracico. H) 2 adenomi delle ghiandole di Zymbal; 1 neurilemmoma del padiglione auricolare; 2 carcinomi mammarii; 1 cistoadenocarcinoma dell'ovaio. I) 1 carcinoma sebaceo della cute. L) 1 adenoma delle ghiandole di Zymbal. M) 1 epatoma a minima deviazione. N) 1 adenoma delle ghiandole di Zymbal; 1 carcinoma delle ghiandole salivari. O) Diversi animali con due o più tumori.

## TABELLA III

*Esperimento* BT3: *Risultati sperimentali a 59 settimane* (1)

| GRUPPI E TRATTAMENTI | ANIMALI (RATTI SPRAGUE-DAWLEY) | | ANIMALI CON TUMORI | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Totale | Sopravvissuti | Carcinomi delle ghiandole di Zymbal | Nefroblastomi | Angiosarcomi: Fegato | Angiosarcomi: Altre localizzazioni | Altri tipi e/o localizzazioni | Totale (2) |
| | N. | N. | N. | N. | N. | N. | N. | N. |
| I) CV 10.000 ppm | 60 | 36 | 3 (11) | — (2) | — (2) | — | — (4) | 3 (15) |
| II) CV 6.000 ppm | 60 | 48 | 1 (3) | — (2) | — (3) | — (1) | — | 1 (9) |
| III) CV 2.500 ppm | 60 | 54 | — (2) | — (1) | — (1) | — | — (1) | — (5) |
| IV) CV 500 ppm | 60 | 56 | — (1) | — | — (1) | — | — | — (2) |
| V) CV 250 ppm | 60 | 44 | — | — | — (1) | — | — | — (1) |
| VI) CV 50 ppm | 60 | 50 | — | — | — | — | — | — |
| VII) Nessun trattamento . . . . | 190 | 183 | — | — | — | — | — | — |
| TOTALE . . . | 550 | 471 | 4 (17) | — (5) | — (8) | — (1) | — (5) | 4 (32) |

(1) Tra parentesi viene indicato il numero di tumori riscontrati nell'esperimento BT1, dopo 59 settimane. (2) Alcuni animali con due tumori.

## TABELLA IV

*Esperimento* BT6: *Risultati sperimentali a 34 settimane*

| GRUPPI E TRATTAMENTI | ANIMALI (RATTI SPRAGUE-DAWLEY) | | ANIMALI CON TUMORI | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Totale | Sopravvissuti | Carcinomi delle ghiandole di Zymbal | Nefroblastomi | Angiosarcomi: Fegato | Angiosarcomi: Altre localizzazioni | Altri tipi e/o localizzazioni | Totale |
| | N. | N. | N. | N. | N. | N. | N. | N. |
| I) CV 30.000 ppm | 60 | 60 | 2 | — | — | — | — | — |

TABELLA V

*Esperimento* BT5: *Risultati sperimentali a 68 settimane*

| GRUPPI E TRATTAMENTI | ANIMALI (RATTI SPRAGUE-DAWLEY) | | ANIMALI CON TUMORI | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Totale | Sopravvissuti | Carcinomi delle ghiandole di Zymbal | Nefroblastomi | Angiosarcomi: Fegato | Angiosarcomi: Altre localizzazioni (1) | Altri tipi e/o localizzazioni | Totale |
| | | | N. | N. | N. | N. | N. | N. |
| I) CV 10.000 ppm Fattrici . . . . | 30 | 28 | — | — | — | — | — | — |
| II) CV 6.000 ppm Fattrici . . . . | 30 | 28 | — | — | — | — | — | — |
| III) CV 10.000 ppm Nati . . . . . | 54 | 50 | — | — | — | 1 | — | 1 |
| IV) CV 6.000 ppm Nati . . . . . | 32 | 30 | — | — | — | 1 | — | 1 |
| TOTALE . . . | 146 | 136 | — | — | — | 2 | — | 2 |

(1) Sottocute.

2) esiste una relazione tra dose e risposta;

3) i nefroblastomi e i tumori delle ghiandole di Zymbal possono essere bilaterali;

4) gli angiosarcomi epatici sono policentrici;

5) in animali trattati, sia portatori di angiosarcomi o no, sono frequentemente presenti alterazioni vascolari diffuse a vari tessuti ed organi, consistenti in proliferazione endoteliale semplice, distipica e francamente atipica. L'azione oncogena sui vasi va ritenuta pertanto un effetto sistemico;

6) l'osservazione di tre angiosarcomi ossificanti suggerisce nuovi spunti per una diversa interpretazione patogenetica dell'acrosteolisi in operai esposti all'azione del CV;

7) fino ad oggi nei ratti da noi trattati non abbiamo osservato lesioni acrosteolitiche.

Carcinomi delle ghiandole di Zymbal, angiosarcomi epatici ed extraepatici, e nefroblastomi non sono mai stati osservati in animali non trattati della nostra linea di ratti Sprague–Dawley. I soli tre casi noti di carcinomi delle ghiandole di Zymbal, in ratti non trattati, furono riscontrati dal dott. Tannenbaum *e coll.* nel 1962; si trattava di ratti Sprague–Dawley.

TABELLA VI

*Esperimento* BT4: *Risultati sperimentali a 34 settimane*

| GRUPPI E TRATTAMENTI | ANIMALI (TOPI SWISS) | | | | | | ANIMALI CON TUMORI | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Trattati | | | Sopravvissuti | | | Adenomi e adenocarcinomi del polmone | Adenocarcinomi della mammella (1) | Angiosarcomi del fegato | Altri tipi e/o localizzazioni | Totale (4) |
| | ♂ | ♀ | Totale | ♂ | ♀ | Totale | N. | N. | N. | N. | N. |
| I) CV 10.000 ppm | 30 | 30 | 60 | 8 | 18 | 26 | 12 | 5 | — | 3 (2) | 13 |
| II) CV 6.000 ppm | 30 | 30 | 60 | 11 | 21 | 32 | 12 | 4 | 1 | 2 (3) | 13 |
| III) CV 2.500 ppm | 30 | 30 | 60 | 13 | 24 | 37 | 6 | 2 | — | — | 6 |
| IV) CV 500 ppm | 30 | 30 | 60 | 14 | 26 | 40 | 8 | 1 | 2 | — | 9 |
| V) CV 250 ppm | 30 | 30 | 60 | 23 | 21 | 44 | 4 | 2 | — | — | 5 |
| VI) CV 50 ppm | 30 | 30 | 60 | 16 | 26 | 42 | — | 1 | — | — | 1 |
| VII) Nessun trattamento . . . . | 80 | 70 | 150 | 61 | 61 | 122 | — | — | — | — | — |
| TOTALE . . . | 260 | 250 | 510 | 146 | 197 | 343 | 42 | 15 | 3 | 5 | 47 |

(1) Nelle femmine. (2) 1 carcinoma squamocellulare, 1 cheratoacantoma e 1 emangioma della cute. (3) 1 linfosarcoma timico, 1 carcinoma nasoparietale. (4) Diversi animali con due o più tumori.

A nostra conoscenza sul ratto non sono mai stati riportati nefroblastomi e angiosarcomi epatici spontanei.

I nefroblastomi non sono mai stati provocati sperimentalmente.

Angiosarcomi epatici sono mai stati indotti sperimentalmente nel ratto con dietilnitrosamina (Reuber e Lee, 1968; Hadjiolov, 1972).

Nel topo angiosarcomi epatici ed extraepatici sono stati indotti con *o*-aminoazotoluene (Andervont *e coll.*, 1942; Andervont, 1950) e con *p*-dimentilaminobenzene-1-azo-2-naftalene (Mulay e Saxén, 1953), e con altri agenti tra cui uretano, dietilnitrosamina, dimetilnitrosamina e dimetilidrazina.

Nel coniglio angiosarcomi sono stati provocati con thorotrast (Zeitlhofer e Speiser, 1954).

Nell'uomo gli angiosarcomi sono rari. Landells nel 1958, facendo il punto sulla situazione degli angiosarcomi descritti in letteratura, ne raccoglieva 117 casi, di cui solo 21 epatici. Essi però sembrano andare aumentando in questi ultimi tempi.

In letteratura sono stati riferiti nell'uomo, 1 caso di angiosarcoma epatico da infissione di radium (Ross, 1932) e numerosi casi di angiosarcomi epatici da thorotrast (MacMahon *e coll.*, 1947; Lüdin, 1953; Da Silva Horta *e coll.*, 1965) e da arsenico (Roth, 1957).

Non appena ci fu chiaro, circa 1 anno e mezzo fa, che il CV esplicava l'azione oncogena su riferita, ne demmo immediata comunicazione non solo alle Società del Gruppo Cooperativo Europeo, ma anche alle altre maggiori Società produttrici del mondo.

I nostri dati hanno orientato l'osservazione clinica e l'indagine epidemiologica.

Alla fine di dicembre del 1973 un operaio di una fabbrica americana di CPV veniva a morte per epatopatia.

L'autopsia rivelava trattarsi di angiosarcoma epatico.

L'indagine retrospettica condotta in queste ultime settimane ha portato al riscontro di 8 casi analoghi (7 degli USA e 1 in Gran Bretagna) di angiosarcomi epatici, che in passato o non erano stati correttamente diagnosticati o comunque non correlati con l'esposizione lavorativa (figg. 7, 8). Tale numero è destinato ad aumentare.

Negli USA e in Germania alcuni operai esposti al CV, con epatopatia sospetta, sono ora sottoposti a costante osservazione.

A conclusione vogliamo auspicare che saggi sperimentali di cancerogenicità diventino una regola prima che venga approvata l'immissione nell'ambiente di nuovi agenti, e che si lavori di più in tal senso e meno nella scolastica discussione (spesso occasione di Comitati e Congressi) sulla validità ed estrapolabilità all'uomo di risultanze sperimentali a cui mancano troppo spesso requisiti di base.

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## SPIEGAZIONE DELLE TAVOLE I-II

### TAVOLA I

**Fig. 1.** – Carcinoma delle ghiandole di Zymbal, scarsamente differenziato, di tipo solido, in ratto esposto a CV. Ematossilina-Eosina. ×125.

**Fig. 2.** – Nefroblastoma, in ratto esposto a CV. Ematossilina-Eosina. ×125.

**Fig. 3.** – Angiosarcoma epatico in ratto esposto a CV. Ematossilina-Eosina. ×125.

**Fig. 4.** – Angiosarcoma epatico in ratto esposto a CV. Ematossilina-Eosina. ×125.

### TAVOLA II

**Fig. 5.** – Angiosarcoma ossificante laterocervicale in ratto esposto a CV. Ematossilina-Eosina. ×125.

**Fig. 6.** – Angiosarcoma ossificante laterocervicale in ratto esposto a CV. Ematossilina-Eosina. ×315.

**Fig. 7.** – Angiosarcoma epatico in operaio addetto alla produzione di CPV. Ematossilina-Eosina. ×125.

**Fig. 8.** – Angiosarcoma epatico in operaio addetto alla produzione di CPV. Ematossilina-Eosina. ×125.

# P R O C E E D I N G S

JUDGE SMITH: This is an informal hearing which is being conducted to give interested persons an opportunity to present oral and written data, views and/or positions regarding the Proposed Temporary Standard for Occupational Exposure to Vinyl Chloride.

Notice of this hearing was initially published in the Federal Register on May 10, 1974, found in 39 Federal Register 17136, and subsequently amended to provide for this proceeding in the notice published on May 24, 1974, in Volume 39, Federal Register 18290, pursuant to the Occupational Safety and Health Act of 1970.

As indicated during the pre-hearing conference, the Administrative Law Judge presiding at this hearing is Gordon J. Smith.

With regard to my function here, it is to regulate the course of these proceedings, dispose of any procedural requests, and confine the presentation to matters which are pertinent to the requested information, and also, in the exercise of my discretion, to determine the extent of questioning of any witnesses appearing here.

I wish to stress, however, that it is not my function to pass upon the evidence which is presented here, but, rather, upon the close of this hearing and after the receipt of any written data or documents submitted within the time which I

will specify at the conclusion of these proceedings, I will certify the complete record to the Assistant Secretary of Labor, Occupational Safety and Health, for his action.

The Official Reporter makes the only transcript of these proceedings and all oral presentations and examinations will be recorded by the reporter.

We ask that any written submission made here be in duplicate and copies of all written submissions and documents received into evidence will be available for your inspection during business hours and before and after each session.

If you desire to purchase copies of the transcript, you must make your own independent arrangements directly with the reporter.

Now, at this point in terms of our order of presentation, if you've picked up a copy of the tentative schedule you will note that first the Department of Labor will make an appearance and a presentation, followed by the National Institute for Occupational Safety and Health, known to you, I guess, as NIOSH, and then we will proceed further with the witnesses as scheduled here, keeping in mind that we are allowing for some flexibility and for some rescheduling during the course of this proceeding because of time constraints which are made known to us.

And I again remind you that if you do have a time constraint, although this doesn't indicate that we can satisfy

your needs completely, let us know so that we can attempt to work something out for you.

On behalf of the Department, there will be an appearance made, and you proceed, please.

[MR. KLEIN: My name is Edward Klein, K-l-e-i-n. Seated to my left is David Kuchenbecker, K-u-c-h-e-n-b-e-c-k-e-r. We are from the Solicitor's Office and we will be representing the Government in this case.]

On behalf of Secretary Brennan and Assistant Secretary Stender, I would like to welcome everyone to this proceeding.

[I should note that the Assistant Secretary of Labor has only issued a proposed standard and that the purpose of the various comments in this hearing is to gather sufficient information to allow him to make an informed decision as to what the final standard will be.

Accordingly, my function and that of Mr. Kuchenbecker at this hearing is to elicit relevant information so that the Assistant Secretary may have the benefit of the knowledge and the expertise of those who testify.]

As a preliminary matter there are certain documents that I would like to introduce into evidence. A list has been prepared of the documents. I will very briefly go through them.

The first exhibit, Exhibit 1(a) through (g) are the various Department of Labor news releases regarding the proposed standard and the fact finding hearing and the like.

Nos. 1 through 9 for identification and were received in evidence.)

JUDGE WHITE: Is that all, sir?

MR. KLEIN: Yes, Your Honor.

JUDGE WHITE: Does the Department wish to make any other statement, or do you wish to go to NIOSH?

MR. KLEIN: Your Honor, at this time I would like to introduce Daniel F. Boyd, the Director of the Office of Standards Development for the Occupational Safety and Health Administration.

[MR. WHITE:] Thank you, Mr.

Good morning, Judge Hyatt, ladies and gentlemen.

[I'm Dan Boyd, the Director of the Office of Standards Development for the Occupational Safety and Health Administration in the United States Department of Labor.

My academic background consists of several degrees in Chemical Engineering and a Ph.D. in Materials Science. I have taught at several universities, including George Washington University and the University of Southern California. I have served as a professional consultant to the chemical industry, the Department of Labor, U. S. Army, and the National Bureau of Standards.

In my capacity as Director of the Office of Standards Development, I have been intimately involved with the vinyl chloride issue. I am appearing here today to briefly review the

proposed OSHA standard and discuss its key issues. I will also introduce the testimony of three expert witnesses appearing at the request of the Department of Labor on certain important issues.

Before beginning, I would like to emphasize that while OSHA has proposed a specific standard regarding vinyl chloride, we regard it as just that -- a proposal. It represents our best judgment based on the information available to us on May 10th. The purpose of this hearing and of the various comments to be presented here is to give Assistant Secretary Stender the benefit of your expertise so that he can make a decision on a final standard.]

As I am sure all of you know, [on January 24th, 1974, OSHA was informed by the National Institute for Occupational Safety and Health -- NIOSH -- that the B. F. Goodrich Company reported several of its employees had died from a rare disease, angiosarcoma of the liver. We immediately ordered a hearing regarding possible hazards associated with vinyl chloride, a substance to which these employees had been exposed. The hearing was held on February 15th, at which Professor Maltoni of Bologna, Italy, reported that tumors were observed in groups of animals exposed to concentrations of vinyl chloride as low as 250 parts per million. At that time, no tumors were observed at 50 parts per million.

After the hearing, Union Carbide, Firestone Tire and

Rubber, and Goodyear reported that some employees who were exposed to vinyl chloride had also died from angiosarcoma of the liver. As a result of all of the information then available, an emergency temporary standard was promulgated on April 5th, reducing the ceiling level of permissible vinyl chloride exposure from 500 to 50 parts per million.

On April 15th the Industrial Bio-Test Laboratories of Northbrook, Illinois, working under contract with the Manufacturing Chemists Association, revealed to OSHA, NIOSH, and EPA -- the Environmental Protection Agency -- preliminary results indicating that [illegible] of 200 mice exposed to vinyl chloride concentrations of 50 parts per million developed angiosarcoma of the liver after seven months of exposure.] I have been informed that Bio-Test will present their most recent results at this hearing.

Since the results of the Bio-Test Laboratory findings in animals indicated that exposure to vinyl chloride at 50 parts per million may well constitute a serious health hazard to employees, OSHA on May 10th proposed a level as low as can be detected feasibly, as determined by a sampling and analytical method capable of detecting vinyl chloride at concentrations of 1 part per million with an accuracy of 1 part per million plus or minus 50 percent.

Since that time, Professor Maltoni completed the experiment which he reported at the February fact finding

hearing and, at our request, graciously made the results of that experiment available to OSHA. Since his experiment is obviously significant, I will now read the contents of Professor Maltoni's telegram, addressed to Assistant Secretary John Stender [illegible] days ago:

"Our project on vinyl chloride carcinogenesis includes 11 experiments, one not completely ended, other ones already [illegible] one or two started for months or few years ago. Results to-date already indicate that vinyl chloride administered [illegible] predisposes to rats zymbal gland carcinomas, [illegible] angiosarcomas of liver and other sites; also [illegible] and probably hepatomas and neuroblastomas. [illegible] exposed at 50 parts per million for one year [illegible] for life, [illegible] animals surviving 135 weeks [illegible] treatment [illegible] liver angiosarcomas [illegible] and one nephroblastoma. Moreover in [illegible] female group a subcutaneous angiopericitoma was observed [illegible] these tumors have been observed on control rats [illegible] all [illegible] brain gliosarcomas and angiosarcomas [illegible] other sites, pulmonary tumors, mammary carcinomas and soft tissue tumors. Over 60 mice exposed to 50 parts per million for seven months at the present moment. After [illegible] treatment we have observed nine mammary carcinomas, two liver angiosarcomas, and two subcutaneous angiosarcomas. [illegible] lung adenoma was observed in one control

mouse."

Signed Cesare Maltoni.

Based upon the Maltoni and the Industrial Bio-Test Laboratory experiments and the 19 cases of angiosarcoma found in persons exposed to vinyl chloride, our present judgment is that vinyl chloride is a carcinogenic agent.

In protecting employees from a carcinogenic material, we are operating in an area of many unknowns. For example, we do not know the mechanism by which a chemical carcinogen operates or whether a safe level of exposure can be set. However, the problem of employee exposure to carcinogens is with us today, and it is our responsibility to deal with it as rapidly as possible based upon the best available information.

Drs. Kraybill and Schmidtmann of the National Cancer Institute will present their views on this issue later in the hearing.

At this time I want to re-emphasize that all views presented will be given the most careful consideration in drafting the final standard.

There are essentially five manufacturing processes which involve vinyl chloride or its polymer, polyvinyl chloride, PVC. I will briefly review these stages. The initial stage involves production of the vinyl chloride monomer. Next, the vinyl chloride is polymerized into PVC, which, in turn, is compounded with additives. The fourth stage involves fabrica-

tion, processing of the compounded PVC into a finished or semi-finished product. The final stage involves the use or handling of the fabricated product.]

This description, I realize, is a gross oversimplification, but I expect the various witnesses here today to describe their operations in depth.

[We recognize that exposure and control problems confronting employers in each of the five stages may differ markedly from those confronting employers in other stages. For example, polymerization plants may have different exposure and control problems than compounders or fabricators.]

I will now address myself to the provisions contained in the proposal.

The proposed standard includes all of the stages that I outlined, except for the handling or use of the fabricated product. We proposed "no detectable level" -- again, as defined earlier in my testimony and in the proposal preamble -- as the ceiling exposure level after considering the test data, the human deaths, and our estimation of technical and economic feasibility.

If any of you care to recommend exposure levels other than that which we have proposed, please provide us with all of your supporting data of the facts and reasoning so that we may have the benefit of your views in the development of a final standard.

In any event, the proposal contemplates that if the exposure exceeds "no detectable level," the employer would, as soon as feasible, institute engineering controls and work-practice methods to reduce the concentrations of vinyl chloride below this detectable level. Pending the institution of these controls and workpractices or if they fail to reduce the concentration of vinyl chloride to "no detectable level," continuous flow-and-demand respirators would be required. In cases of emergencies, respirators were also contemplated.

[We recognize that respirators are not popular with employees and that employees may have difficulty wearing them 40 hours per week. However, in balancing the feasibility of engineering controls and workpractices, respirators, and the hazards associated with vinyl chloride, we feel that respirators are a necessary temporary means of avoiding employee exposure to vinyl chloride.] Dr. Bjaki will address the entire question of respirators later in this hearing.

[Some commentors have asked what "feasible" means. Within the terms of this proposal, feasibility refers to both technological and economic considerations. On the one hand, does the technology exist that would allow the employer to achieve compliance and, on the other, what are the costs associated with the application of these technologies. It is both proper and necessary that we consider these matters in our deliberations.] We solicit your assistance in addressing these.

complex issues.

Another area where some questions have arisen is monitoring. I am told that Dr. Key, the Director of the National Institute of Occupational Safety and Health, will discuss this more fully, but let me say our experts agree, for example, that a gas chromatograph is fully capable of measuring vinyl chloride at the levels required by our proposal and is both widely used in the vinyl chloride and polyvinyl chloride industry and available to those who do not now use them.

Please note that we have deliberately refrained from stating specific sampling and analysis methods because we do not want to discourage employers from using improved monitoring equipment as it is developed.

There seems also to be some confusion as to what we mean by a 95 percent confidence level with respect to monitoring. The 95 percent confidence level in the proposal requires the employer to monitor a sufficient number of times so that both the employer and OSHA are confident that the monitoring results are accurate and that employee exposure is accurately determined.

We have essentially proposed a performance standard with respect to engineering controls and workpractices. We recognize that each employer should be allowed to utilize the engineering controls and workpractices which are best suited for his plant.

1 Because each plant differs, it is impossible for me to
2 state the precise engineering controls and workpractices that
3 will be necessary for each employer to comply with the provi-
4 sions of this proposal. However, the proper application of
5 ventilation systems and further reductions of exposure sources
6 appears to be a rational approach. It is entirely possible
7 that a reduction of the 10 to 12 percent unreacted monomer
8 which often occurs at the polymerization stage will reduce some
9 of the vinyl chloride exposure problems associated with the PVC.
10 Perhaps more efficient recycling of the unreacted monomer at
11 the polymerization stage would be helpful in reducing vinyl
12 chloride exposure.
13 I should note that we are aware of the cost asso-
14 ciated with engineering controls, workpractices, and the use of
15 respirators. It is both proper and necessary that we consider
16 these factors in our deliberations. Further, we anticipate
17 that those who testify at this hearing will give us more
18 specific information in this regard.
19 Some commenters have raised the question as to what
20 a "regulated area" is within the context of our proposal.
21 First, let me note that when an area is classified as a
22 "regulated area," monitoring, medical surveillance, labels and
23 signs, and recordkeeping are required. In vinyl chloride
24 operations a "regulated area" exists whenever vinyl chloride
25 is manufactured, reacted, stored, handled, released, repackaged

or not.

In polyvinyl chloride operations a "regulated area" exists only when the polyvinyl chloride is capable of releasing detectable levels of vinyl chloride. This recognizes that there may be operations involving PVC which may be incapable of releasing [illegible] however.

Intermittent cleaning would be required in regulated areas. Since the continual body contact with vinyl chloride has been identified as a cause of acroosteolysis, we assume that vinyl chloride may be absorbed through the skin. Moreover, when vinyl chloride is in a liquid state, the temperature is so low that this content is considered a hazard. I hope that the [illegible] will be presented at this hearing on the question of absorption of vinyl chloride through the skin.

Periodic medical examinations serve two purposes. First, it [illegible] for the early discovery of employee liver dysfunction, and removal of such an employee from any contact with vinyl chloride. Secondly, the medical surveillance records are necessary for epidemiological studies which will no doubt take place. I should note that for the same reasons medical examinations are required for all employees who work in regulated areas, even if there is no "detectable level" of vinyl chloride.

The proposal contemplates that medical records, monitoring and measuring records, and regulated area entry records or summaries thereof be kept for at least 20 years.

Because of the apparently long latency period of angiosarcoma, this requirement is likely to benefit employees, since an accurate medical history is beneficial in diagnosis and treatment. As I pointed out previously, it also serves epidemiological purposes.

We are aware that employers are opposed to labels and signs containing the word "cancer" because of the psychological effects it may have on both employees or applicants for employment. On the other hand, Section 6(b)(7) of the OSHA Act requires "...the use of labels and such appropriate forms of warning as may be necessary to insure that employees are apprised of all hazards to which they are exposed..."

We have proposed signs and labels which indicate that a "cancer-causing agent" is present in regulated areas and on containers which house either vinyl chloride or PVC which is capable of releasing detectable levels of vinyl chloride. Training will convey this message, but we believe signs and labels are necessary to apprise employees of the hazards associated with vinyl chloride.

Some employers have objected to the provision that allows employees or their authorized representative to observe the required monitoring. Since the employees run the risk of exposure to vinyl chloride, it seems to us that they should have the right of observing monitoring and measuring of the vinyl chloride exposure.

In conclusion, I would like to reemphasize that I have presented a proposal to you today. We do not claim to know all the answers on all the problems associated with employee exposure to vinyl chloride. I am here today asking for your help for your input, so that we can promulgate a standard based upon the best and most recent information available.

[illegible] the [illegible] members of the [illegible] Subcommittee on the necessity [illegible] of the emergency temporary standard and the proposed permanent standard.

Mr. Donald Anderson on my right, a Fellow in Environmental [illegible] the University of North Carolina, Chapel Hill, will be available to answer any questions you may have. I'm delighted to have him here, [illegible] the questions are difficult for me to handle, which I'm sure will happen very quickly.

Beside me, Grover Wrenn. Grover, would you stand, please. Dr. [illegible] formerly of the University of North Carolina and the Hill Environmental Group, a very fine industrial hygienist on our staff.

The project officer for vinyl chloride, Gene Vogel. Gene is a good old local engineer.

I could your questions.

Mr. Hill: How [illegible] your questions of Mr. Boyd?

Why don't you bring them up, Mr. Boyd, let's proceed to the mic

of the organization --

MR. CONNOLLY: Your Honor, we'd like to ask a question.

JUDGE LEVEN: Would you come to this microphone and identify yourself, please?

MR. CONNOLLY: My name is Walker D. Connolly, Jr. I'm Labor Counsel to Firestone Tire and Rubber Company.

It's my understanding that your department issued a temporary emergency standard on April 5th, 1974. At that time did you have that standard on the best available information you had?

MR. BOYD: Yes, we did.

MR. CONNOLLY: What information between October 5th, 1973, and May 10th, 1974, did you obtain to base the decision which resulted in the proposed permanent standard? What additional information did you obtain?

MR. BOYD: You used different dates on me. Do you mean --

MR. CONNOLLY: Well, the proposed permanent standard was published on May 10th --

MR. BOYD: Right.

[MR. CONNOLLY: What information did you obtain between April 5th, the date of the temporary standard, and May 10th, the date of the permanent standard? ]

MR. BOYD: Fine. You said October, and I was a

Mr. Boyd --

MR. CONNOLLY: Excuse me.

Mr. Boyd: In my statement the data from the Industrial Bio-Test Laboratories and the data --

MR. WEISS: Mr. Boyd, would you pull the mike closer to you?

Mr. Boyd: The data from the Industrial Bio-Test Laboratories sponsored by EPA.

MR. CONNOLLY: That's the only additional information that you obtained between April 5th and May 10th?

Mr. Boyd: I would have to read the record to see what else I wrote.

MR. CONNOLLY: But, to your recollection, there's nothing else?

Mr. Boyd: That's correct.

MR. CONNOLLY: You indicated -- I believe that your department did a survey or study of some plants in the Southwest; is that not correct?

Mr. Boyd: We have visited natural rubber, polymer, and fabrication plants.

MR. CONNOLLY: Have you been able to discern any distinction or dichotomy between those plants that exist in the Southwest and those plants that exist, for instance, in the Northeast?

Mr. Boyd: The studies have not been that in-depth,

but I might point out one problem that we know. The northern plants, of course, tend, because of the weather, to be indoor plants; whereas, the plants in the warmer climates are open, and I would contemplate less of a problem in an open plant.

MR. CONNOLLY: You anticipate there would be less problems in, for instance, the South or the Southwest than there would be in the North or the Northwest?

MR. BOYD: Yes. I anticipate that, yes, sir.

MR. CONNOLLY: Has anybody from the Department of Labor obtained any engineering or technological studies connected with the building of new plants in this particular industry or the remodeling of old plants?

MR. BOYD: We have looked at it in a cursory manner. We are familiar with the Dawmoor process which uses a large reactor that cures by loss of a problem to vessel entry.

MR. CONNOLLY: Do you know whether or not there was any engineering studies or technological studies done by NIOSH prior to their recommendation to you of the proposed permanent standard?

MR. BOYD: They will testify later, sir, as to that point.

MR. CONNOLLY: But you have no studies yourself?

MR. BOYD: No, sir.

MR. CONNOLLY: Have there been any economic studies done by the Department of Labor to determine the impact of the

changes that would result from the proposed permanent standard becoming permanent?

MR. BOYD: Those studies are ongoing.

MR. CONNOLLY: And who is doing that?

MR. BOYD: The Department staff itself.

JUDGE MIATT: Are there any other questions of Mr. Boyd?

MR. CONNOLLY: When will those studies be available?

MR. BOYD: I don't know at this time.

MR. CONNOLLY: You indicated also that one of the proposed work standards deals with respirators. Has the Department of Labor been involved in any studies as to possible or potential dangers that result from the use of respirators?

MR. BOYD: We have not, but, of course, NIOSH, our sister agency, has and we're fortunate to have with us at this morning one of the world's experts on respirators and he will testify shortly -- later.

MR. CONNOLLY: He'll be testifying?

MR. BOYD: Yes, he will.

MR. CONNOLLY: That's all. Thank you.

JUDGE MIATT: All right. Let's proceed with your next witness on behalf of the Department.

MR. BOYD: At this point I'd like to introduce Dr. Knaybill of the National Cancer Institute. The content of his presentation, I have so entered in the testimony.

Dr. Kraybill.

[DR. KRAYBILL:] Your Honor, Judge Hyatt, Mr. Boyd.

[I am Dr. Herman F. Kraybill, Scientific Coordinator for Environmental Carcinogenesis, National Cancer Institute.

I have a Ph.D. degree in Biochemistry and have broad experience in the field of toxicology; a Master's degree in Physical Chemistry, and a B.S. degree in Chemistry. I've had five years experience in industry and about 29 years experience in the Federal Government, fourteen of the last years being with the U. S. Public Health Service.]

I have the curriculum vitae here, Your Honor, and I will submit this for the record.

JUDGE HYATT: All right. This will be Exhibit No. 10, Media Reporter.

(The document above referred to was marked Department Exhibit No. 10(a) for identification and was received in evidence.)

DR. KRAYBILL: I do not intend to go into great detail about the experimental work that has taken place on the carcinogenicity evaluation of vinyl chloride because that will be covered by other speakers, and this has appeared in various publications, the work of Dr. Maltoni, Professor Maltoni; the work of Professor Viola, and the more recent studies by the NCA supported project at Industrial Bio-Test Laboratories, who I understand will report later on in this hearing.

Rather, I would dwell on certain concepts and principles concerning the carcinogenicity of vinyl chloride. The rare and inevitably fatal form of cancer, angiosarcoma of the liver, now implicates vinyl chloride and the polyvinyl chloride residual monomer in occupational exposure to this chemical, which has previously been shown to induce angiosarcoma of the liver in experimental animals.

What makes these recent reports on occupationally induced cancers of even more significance is the wide usage of the chemical and its production and its economic importance. Only two other chemicals have previously been reported to induce this rare neoplastic lesion; thorotrast, used clinically in cerebral vessel visualization, and an arsenic pesticide used by Carmel vineyard workers.

Both vinyl chloride and thorotrast revealed some suggestive evidence on their potential carcinogenic hazard to man through animal experiments. Arsenicals, however, by contrast has no satisfactory animal models to signal their cancer-inducing properties in man.

The latency period for development of angiosarcoma of the liver in man is comparable for all three etiologic agents.

Earlier studies, about 20 years ago, on vinyl chloride gave some indications that this was a hazardous chemical because of its capacity to cause liver and kidney injury, but its carcinogenic hazard was not realized until the

studies of Professor Viola revealed some cancers of the skin, bone, and lung in rats; the high dose of about 30,000 parts per million -- that would be roughly four hours per day for five days a week for 12 months' exposure -- did not seem to elicit liver cancer. Therefore, there are indications that vinyl chloride may be a carcinogen for sites other than the liver in man and epidemiological studies may uncover these possibilities.

Professor Maltoni, at the Institute of Oncology in Bologna, Italy, in his recent work has indeed confirmed Viola's original work, but in rats his findings extended observations from reports on cancer of the zymbal glands -- that's the inner ear canal -- nephroblastomas and angiosarcomas of the liver and also recently intra-abdominal area angiosarcomas, the latter findings even at the low dose of 50 parts per million after one-year exposure. Vinyl chloride is thus capable of inducing angiosarcomas and angiomas of the liver, and I noted with much interest in this recent wire from Maltoni, Dear Dear Maltoni, that he reported that we may get probably hepatomas.

I'm not a pathologist, but indeed this is of interest to some of us because this implies not only action on the endothelia cells, but action on the hepatocytes, which is a different type of lesion.

The Manufacturing Chemists Association in their supported project at Industrial Bio-Test Laboratories, where

they are doing studies with rats, mice, and hamsters, they have established also that angiosarcomas of the liver appeared in mice challenged with vinyl chloride through inhalation studies. The MCA project is significant in that liver angiosarcomas in mice appeared in as short a period as six to seven months' exposure at 50 parts per million dose of vinyl chloride, doing a study similar to that that Maltoni did, five days' exposure as in other studies, and these studies will be carried on for 12 months.

In a test group of about 200 mice -- I'd like to state here that they say 2 out of 200. It's really 40 animals that were cannibalized or died and of about 18 of these that were examined, two had liver angiosarcomas, so on a percentage base that ran it somewhat high. Since the MCA project is still continuing with a longer exposure period extending to 12 months, it may be anticipated that there will be a higher incidence of angiosarcomas for those exposed at the 50 parts per million level of vinyl chloride, and I'm sure we'll hear about that later from the MCA investigators.

Therefore, data from several laboratories fulfills the requirements for a proven carcinogen in that observations were made on angiosarcomas of the liver in several species and strains and there follows a good dose-response relationship, with most recent data showing a response at as low as 50 parts per million.

With a larger population of animals carried beyond a seven-months period, as in the MCA study, it might be expected that the over-all incidence could perhaps reach the order of 5 percent. Additionally, it would not be surprising if a response as to liver angiosarcoma would be elicited at levels below 50 parts per million, if we used a larger animal population.

At 50 parts per million exposure level, the time frame of six months for induction of angiosarcomas of the liver in mice is rather, to put it mildly, unsettling in that long-term continuous exposure, comparable in experimental animals to a time frame for human occupational exposure, may reveal angiosarcomas of the liver at an extended induction period which in man could mean a period perhaps beyond 20 years.

I note on the charts, that the induction period ranges anywhere, for the 19 people, from eleven to about thirty years.

If one were to assume that in a population occupationally exposed to vinyl chloride there were 100,000 workers involved in such operations as synthesis of vinyl chloride, transporting vinyl chloride, polymerization of vinyl chloride to polyvinyl chloride, and fabrication and storage of PVC with residual VC monomer present, then perhaps a 5 percent incidence would be most significant for workers at risk.

Such risks do not include those that may arise in non-occupational situations such as polluted air, water, and

previously the use of aerosolized products containing VC as a propellant -- I presume someone will address themselves to this point on the environmental contamination problem, but as an environmental health scientist, I always indicate that one has to consider several types of stresses. The stress that the individual man or woman gets in the general environment by inhalation of the air, the drinking of the water, and the diet, and, lastly, he gets a superimposed stress on top of that which is the stress in the exposure in the workplace. That's what I call the total or integrated stress.

Unfortunately, we do not have at hand the epidemiological data relating acute exposure levels to VC with occurrence of liver angiosarcomas in man. Earlier estimates of exposure levels to VC for plant workers in the past -- and I quote some data taken from a NIOSH representative where he indicated that they may range from 1,000 to 2,000 parts per million and higher. Reports have been received about angiosarcomas of the liver in people not directly receiving plant exposure to vinyl chloride.

Based on what facts we have given, vinyl chloride appears to be a potent hepatocarcinogen. It is capable of inducing non-neoplastic lesions and liver dysfunction, culminating in the irreversible angiosarcoma of the liver. If man responds to low level exposure to vinyl chloride as has the rodent, a low level, continuous exposure of 50 parts per

million for man would have a high probability for inducing liver cancer.

Certainly, there is little margin for safety if a response can be expected at a level below 50 parts per million, which in truth is now only a fifty-fold safety factor in terms of the proposed standard. According to toxicological principles, were this compound a noncarcinogen, then to establish a tolerance or safe level, there would have to be a 100 to 1 margin of safety in terms of a no-effect level, and from the experimental data on the animals we don't even know yet what the no-effect level is. Obviously, this would put the allowable level at a small fraction of a given standard -- of the given standard. Scientifically -- and this is not pragmatically but scientifically for a carcinogen one would like to see an exposure level that approaches zero. The proposed standard, however, attempts to achieve, as far as possible within engineering and technological feasibility, a very low order of exposure.

Beyond these attempts to maximize worker protection from vinyl chloride exposure, there are other factors that may be associated with exposure to this hepatocarcinogen. Our knowledge concerning the role of associated contaminants in vinyl chloride in the induction of cancer at various sites, especially the liver, is lacking as is the role of dietary stress such as low protein intake and the insult from alcohol

which could accelerate the formation of the neoplastic lesion or indeed reduce the latency period.

In the pathogenesis of liver cancer evoked by vinyl chloride, some other details are still unknown. For example, little is known about the precancerous lesions and the progression of these lesions within a time frame as morphological changes finally are recognized as the irreversible angiosarcoma induced by vinyl chloride. Dr. Maltoni alluded to this in his work and so did Dr. Popper.

Much of this experimental work was done by giving the animals repeated inhalations vinyl chloride on a continuous exposure basis for four days for six or seven months, going to lesser numbers of a year, but we don't know really what would happen if there were a pulse dosing for a couple days with a cessation for a short period of time. We don't know really much about the pathology of what happens preceding the development of this irreversible neoplastic lesion.

Such information is needed in order to ascertain whether the process can be interrupted or reversed. Additionally, pharmacokinetic studies may provide a clearer picture of the pathogenesis of this lesion in terms of time and dose-response relationships which may afford, hopefully, some effective measures for cancer control.

THE CHAIR: Thank you, Dr. Brayhill.

I take it that Dr. Schneiderman is your next witness.

I'm going to hold to the original procedure, and I'm going to ask that a panel complete its direct testimony before any questions of the panel.

Dr. Schneiderman.

MR. BIRD: Yes, sir. Dr. Schneiderman of the National Cancer Institute, a biostatistician, is our next witness.

[DR. SCHNEIDERMAN: I'm Marvin Schneiderman of the National Cancer Institute. I'm the Associate Director of the Institute for Mathematical Studies and Statistics.

I was born in New York City, as some of you may have already recognized. I was undergraduate at City College of New York, and I eventually got a Doctor's degree from the American University here in Washington, D. C. I've also done graduate work at Harvard University, at Ohio State, London School of Hygiene and Tropical Medicine, where I was a Rockefeller Public Service Fellow.

My particular interests, my major interests have been in problems of human experimentation, the mathematics of human experimentation, and the ethical problem of human experimentation. In particular, I have worked on controlled clinical trials; I have worked on problems of extrapolation from mouse to man, and I discovered I've plagiarized myself -- I've written two papers with that title, "From Mouse to Man," one on treating cancer and one on attempting to extrapolate

experimental data on materials that produce cancer from the animal experimentation to man.

I'm an editor or have been an editor of "Cancer Research," the journal of the National Cancer Institute; of "Blood," which is the journal of hematology; of the journal "Biometrics," which is a statistical journal covering statistical problems in biology in medicine.

I'm a member of a great many scientific societies, which deal on a lot of fora each year, and I've taught at Georgetown University's Medical School, the University of Pittsburgh Graduate School of Public Health, at the University of Miami Medical School, the Graduate School of the United States Department of Agriculture, and several other places.

With the Cancer Institute I have a group of roughly 90 people that work with me, about ten medical doctors, about ten persons who are doctors of philosophy in various areas, mostly in nutrition and statistics. The physicians are largely epidemiologists. We are concerned with the problems of epidemiology of human disease, with the mathematics of experimentation, with the problems of experiment design, and the problems of data gathering.

I'll talk here today -- I'll try to give information largely related to the problem of extrapolating animal data to human data. The remarks that I'm going to make are very close to those that I made at the meeting at New York Academy of

Science [illegible] with which concerned itself with the problem of vinyl chloride and polyvinyl chloride.

From the point of view of the mathematician or the statistician working on the problem of extrapolation of animal data which are generally obtained at moderate or high doses in order that we might be able to conduct some relatively small experiments and still get some responses to the problem of extrapolation to very low doses, this problem which I call the "No Model" problem, is a problem like simply in the choice of the mathematical model of the dose-response curve. What does it matter if the response curves look like one in the range in which we actually have our observations.

Say you would do extrapolation in a region in which you do not have observations, and then you want to know what it is at very much lower dose levels.

There are three or four mathematical models that are in use by biologists and toxicologists in this particular area and the curves of four different models give you within the range of data from 2 percent to about 98 percent response [illegible] sensitivity, that is, in the 2 percent to 98 percent response range, all the mathematical models seem to all fit the data equally nicely.

The problem then is what happens down below the 2 percent range, which of these models should we use when in the data in which we can observe ourselves we can't distinguish on

1 really [illegible] very nearly, even for these particular models.
2 The models are essentially these: there is a model
3 which says that everyone in the world -- and now I'm talking
4 about experimental animals -- every experimental animal that we
5 work with comes from a population which has a different thres-
6 hold of sensitivity. The threshold of sensitivity may be very
7 low for certain animals. In other words, these animals are
8 very sensitive to the material, and in some animals it may be
9 very high.
10 One shape of the curve describing the threshold of
11 sensitivity is the so-called [illegible], bell-shaped curve, the
12 Gaussian [illegible] curve -- things that people used to complain
13 about when they were in school, that they were marked on a
14 curve, that's the curve. It's probably best known to us as the
15 curve of distribution of height for persons of one sex and one
16 ethnic group, a nice, symmetric, bell-shaped curve.
17 Another one of the models that's used is the so-
18 called -- this particular model, as I say, is called the probit
19 model, probit for probability. The probability of an event
20 occurring is the probability of how many individuals are below
21 that threshold level.
22 Another one of the models in use is the so-called
23 [illegible] logistic model, and this is a model derived from
24 chemical kinetics. It's one which says that at very low doses,
25 a very slow increase of response; then as the dose is increased,

the response increases very rapidly, and then at very high doses, the increasing number of individuals that will respond flattens out. This, as I say, is derived from concepts in chemical kinetics or concepts in binding theory, in the way carcinogenesis operates. It says that there are a small number -- there are a number of binding sites on the cell which the chemical has to attach to in order to have an effect, and after a while flattening out at the top levels indicates that most of the binding sites or almost all the binding sites have been used up, chemicals have attached to them, and the chemical has to go around hunting for additional binding sites, so the chemicals then become far less efficient in producing its effect.

Another one of the models in use, the so-called "one hit" model or the generalization, the "hit-miss" models, which says that in order to produce a carcinogenic effect, a cell has to be hit by a bundle of energy, a quantum of energy, a bundle of chemical, or something of that sort, and one hit is enough to convert the cell from its normal functioning behavior to a cell which is now a cancer cell and which goes on in its own merry way but is not subject to the usual controls that normal cells have.

The one-hit models are modified into a whole group of related models, two-hit models -- it doesn't take one blow to cause this effect, it takes two blows to cause this effect.

There isn't just one mechanism in the cell that has to be turned off or turned on, there are two mechanisms in the cell.

And then, finally, there are a whole group of models called the extreme value models, and the kind of problem we're concerned with here is an extreme value problem, what occurs at the very low levels, the extreme value of dosing. These extreme value models have their counterpart in engineering: the engineers attempt to build a dam so high that the highest flood in a period of a large number of years -- let's say 200 years or 250 years -- will not exceed the height of that dam, an extreme value concept.

The extreme value models and the so-called hit-miss models seem equally at the very low doses. They turn out to be essentially the same thing at the very low doses.

When we consider, then, extrapolating the data that one gets in the mid-range of experimentation, the 2 percent to 98 percent response levels such as the kind of material that's been alluded to here earlier today, the work that Maltoni has done, the work that other people have done. You're then faced with the choice of one of these particular models. The different models give you very different results at the very low dose levels.

The one-hit model, which is the one that's currently accepted for the problems of the induction of cancer through radiation, through atomic energy, gives you results down at the

very low levels that are -- give you so-called safe doses, down at the very low levels of exposure that are very much lower than do the probit or logit models -- that is, the one-hit model requires a very much lower dose to be called safe than does the probit model to be called safe.

Several people have attempted to provide some logical reasons for using one or the other of these models. One of them is my colleague Nathan Mantell, who is now with George Washington University, and in 1961 he and Ray Bryan, a cancer researcher, developed a model, the so-called Mantell-Bryan model, which uses as its basic theory the probit dose response curve, that is, the least conservative of the curves -- the one that gives you the highest safe level. Then imposed on this particular probit dose response curve a so-called guarantee level, an upper level -- your responses have been, let's say, two out of fifty or three out of fifty or something of that sort, and they say, "Now, in experimentation, two out of fifty is consistent with a very much larger number having occurred, but in this particular small experiment, this is what we have got. Let's be careful and be conservative and erect either a 95 percent upper confidence limit or a 99 percent upper confidence limit on this particular observed response, and then let us extrapolate down from that level, also taking into account the effects at higher dose levels." Let us extrapolate down from that dose level to whatever level we say is a safe level. From

that dose level, let us say, for example, down to a level -- we've seen two and fifty -- down to a level that will produce for us one in a million responses or one in a hundred million responses" -- whatever level, in some sense, society decides is a virtually safe level.

For extrapolating down to the very low responses, Marshall and Hoyer recommend using a slope in this dose response curve of one unit, one probit unit per tenfold dilution of dose. They recommend this because there are biological data which would seem to indicate that this is a suitably conservative dose. There are biological data which would indicate that there are suitably conservative slope -- there are biological data which indicate that this slope of one per tenfold dilution may not be sufficiently conservative. There are some data in man -- for example, the smoking in lung cancer data -- which would indicate that the slope is shallower than that.

The shallower slope that you have, the lower becomes the dose which can be considered safe. You have to go much further out on the scale to come down to a dose that's considered safe.

Now, with these particular concepts in mind, I've asked one of my colleagues, Dr. Brown, to take the Maltoni data as of last week before the telegram came that Dr. Kraybill alluded to -- to take the Maltoni data and make some computations as to what would be for the Sprague-Dolley rat -- because

that's the animal that Melton worked with -- what would be a level of dose that would produce a risk of, let us say, one part per 100,000, one part per million, one part per ten million, one case in ten million, one case in a hundred million.

McClure

The results of Brown's computations are as follows, and I'll give some material which essentially will be in tabular form, in which, across the top of your table, I will label "Risk Level."

In the first column down in that will be 1 in 100,000. The next column will be one in a million, the next one in ten million, and the next, one in one hundred million.

Now, in the stub of the table I will list the extrapolation models that I am using, and the first one will be the Mantel-Bryan procedure, the second one will be the so-called logistic model, with a fairly steep slope -- 3.54. The next will be a logistic model with a slope of 2.3, and the next will be to the so-called one-hit model.

The logistic model with the slope of 2.3 and the one-hit model are essentially equivalent.

Now, the numbers that I am going to give you are the parts per billion -- the parts per billion -- which will produce these particular risk levels that I have stated, given the data of Professor Maltoni with the Spraig-Dooley rats as of the beginning of last week.] I had hoped to have for you today the further computations based on Professor Maltoni's telegrams, and while the Italian Postal Service is now back at work, the National Institutes of Health computer was having some hiccoughs yesterday and we couldn't do it. That's not a technical diagnosis: the hiccoughs in a computer!

WJD-2

The results in this particular table: the parts per billion that would produce, under the Mantel-Bryan model a risk of one in one hundred thousand; 251 parts per billion would produce a risk in the Sprague-Doiley rat of one in one hundred thousand.

I am now reading across. One in a million, 81.6 parts; one in ten million, 29.2 parts. One in one hundred million, 11.3 parts.

For the Logit model with the steep slope, the same column headings, 574, 124, 26.7, 5.74.

For the Logit model and the one-hit model in the range in which they are essentially equivalent, for a risk of one part in a hundred thousand, 24 parts per billion. For one in a million -- and this goes down, you'll notice, strictly linearly -- one in a million: 2.4, one in ten million: .24, one in a hundred million: 0.024.

Now, these are, as I say -- these are the extrapolations down to the very low levels of risk that the Maltoni data, the first experiment that was described here, the BT-1 data, would imply.

We have not done similar computations for the data from the Manufacturing Chemists Association for several reasons; one, I have not actually gotten the experiment, the material, protocol -- the results. As someone who is concerned with this particular kind of thing, I personally am disturbed

at the very high mortalities that have occurred very early in that experiment, and I am concerned about whether one has to make some adjustments for these very high mortalities before these computations can be done.

So we have not made these computations.

The new data that derives from Professor Maltoni, the material that came late last week, which indicates that at the level of 50 parts per million there were now three tumors found in the last three animals that died, would lower all these particular estimates that I have shown, would lower the safe levels for these various safety levels lower than what I have already given you.

So where I got 250 parts per billion for the Mantel Bryan model, for a risk of one in one hundred thousand, the new data would probably indicate that somewhat under 200 parts per billion.

Now, there are several other ways of extrapolating other than the ones that I gave you. The classical toxicologist -- by and large, not the cancer people, the people who have been involved in other kinds of risk problems -- look for a so-called "no-effect" level, the level at which no response has been seen, and in general, will divide that level by 100, sort of building in an engineering safety factor, as it were, and say that then would be a safe level.

From the last weeks Maltoni data, that would have

given you, as a safe level by the classical method, 500 parts per billion. That is, there had been no response at 50 parts per million, you divide that by 100 to give you 500 parts per million.

Carol Wyle, a research experimenter who has been concerned with these problems, who is at the Carnegie-Mellon Institute, and I believe with the Union Carbide Company, has recommended that one take the lowest level at which any response occurs and divide that by roughly 5,000. Well, that would mean taking the early Maltoni data, the 250 parts per million, dividing that by 5,000; that would give you, by Wyle's technique, 50 parts per billion as a safe level, if my arithmetic is correct.

After one has done this -- now, these are safe levels for Sprague-Dawley rats; after one has done this, and computed these levels for rats, then something has to be done to translate that into risk-levels for man.

Several people have worked on this particular problem, and by and large, it would appear that most people would like to add some additional safety factors when converting from rats or mice to men.

In addition, there are some concerns about how one measures the dose. Doses are often measured on a miligram per kiligram basis, but there is some evidence to indicate that perhaps the dose ought to be on a miligram per square

meter basis, a surface measure rather than a weig ht measure. There is some historical experiment in which converting from a small animal to a large animal on a miligram per kilogram basis has led to some disastrous results.

The mouse or the rat -- the rodent's circulation is very much more rapid in terms of the time that it takes to circulate his total blood supply than is man's. This would seem to imply that the same dose at equivalent size should be more carcinogenic for man than it is for the mouse or rat. It stays in man longer, in terms of how it circulates through his body.

When all these considerations are taken into account, I suppose we also have to add that the experimental animals are generally inbred animals, genetically quite similar, without the great range in response rates that one has in humans, without the great diversity that one has in humans, and when one considers that our problem is probably to protect sensitive humans -- the more sensitive humans who will then be responsive at very much lower dose levels, some additional safety factors of the engineering factor type probably have to be added into the information we got from the mouse levels. The mouse and rat levels.

These generally run -- from people saying:

"Well, divide whatevr it is you get for the mice or rats by 100..."

like the classical toxicologists, to people who insist that that is not nearly not enough, that you must divide by 1,000 and some people have indicated that you must divide by considerably more than that.

I don't know -- I have no specific recommendations concerning the safety factor that one should apply from mice to men, other than to indicate that the numbers that I gave you in the previous table are extrapolating from rat to rat, or in mouse experiments, I call this "in-mouse" extrapolation; to do out-mouse extrapolation from the mouse to man probably implies dividing these by something at least of the order of 100 and perhaps as much as the order of 1,000.

There are other ways to extrapolate from experimental animals to humans, but none of the data that have been developed so far, that have been reported on so far, are sufficient or satisfactory to use these other methods.

I will mention one and indicate the kind of data that we would like to see and which perhaps will be available in this problem, so that we might be able to use this method.

Quite obviously, everybody has to die from something. The question then should be, not how many people have died from this particular form of cancer, but really, how much earlier in their lifetimes have they died from this form of cancer than had they not developed this form of cancer?

And so what you need to know then is the time from

exposure to the time of appearance of the disease, or the time of death -- from the disease, rather than just the fact that the disease occurred or/it did not occur.

The data that have been presented so far, developed so far, have not, in the public reports, have not produced this particular kind of information, so it is not possible for us to go through these kinds of computations.

I would like to give you a sort of sense or feeling as to what -- when we do these computations, what they might mean, sort of give you a sort of keystone or a trigger, or opening the look to the magnitude of these differences that occur.

All of cancer -- all of cancer, and cancer is the second leading cause of death in this country -- all of cancer reduces life span at birth -- if there were no cancer in the world, the child who was born yesterday would have a lifespan two years longer than he has, now that he has been born into a world in which there is such a disease as cancer, which in this country is the second leading cause of death.

This then means, if we make computations in relation to environmental insults of this particular type, we may get numbers of the order of shortening from time of birth of minutes, but that has to be considered in relation to the fact that all of cancer is reducing lifespan at birth by two years.

For the person who develops cancer, quite obviously

the shortening is very much greater. For a disease such as lung cancer, which for the whole population would reduce lifespan -- if there were no such thing as lung cancer, would, say, reduce lifespan on the order of about, I think four months, for the person who develops lung cancer, this reduces his lifespan on the order of eight to ten years.

So this is another measure and another way of looking at it.

As I say, experimental data are not in such shape as to make these computations at this time, so I have not talked directly to the results of these particular other methods of extrapolation.

Thank you, sir.

JUDGE HYATT: Doctor Schneiderman, do you have your oral presentation in a written form?

DOCTOR SCHNEIDERMAN: I have a preliminary copy of the manuscript, based on the materials I presented at the New York Academy meeting, and with your permission, sir, I would like to edit this. I have gone through it and I find that there are typographical errors and things of that sort, and then I will make it available to you.

JUDGE HYATT: All right; we will designate that as Exhibit No. 11 and reserve a place in the Exhibit File for it, when we get it in its edited version.

[Document marked Exhibit No. 11.]

CX 11

TESTIMONY ON:

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PROPOSED STANDARD FOR OCCUPATIONAL

EXPOSURE TO VINYL CHLORIDE

BY:

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BASED ON:

Remarks made at the New York Academy of
Sciences Working Group on Toxicity of Vinyl
Chloride, Poly-vinyl Chloride, New York, New York
May 10-11, 1974 and to be published in
The Annals of the New York Academy of Sciences

June 25, 1974

There are difficult problems in extrapolating the results of animal experiments to possible results in man. Small animal experiments done at moderate to high doses must be used to tell us about what is likley to happen in a very much larger population of humans exposed at (hopefully) substantially lower doses.

The usual way to extrapolate to responses at low doses is to assert the existence of some mathematical model of dose-response and then compute the response at the desired dose or compute the dose for the desired response.

Presently two classes of mathematical models are advocated for in-mouse extrapolation. There are the models that deal with yes-no data, the dichotomous data models. These are concerned with whether or not an effect occurred.

The data presented by Professor Maltoni in his experiment BT-1 after 52 weeks of exposure and 130 weeks of observation are of the yes-no type:

| | ANGIOSARCOMAS | |
|---|---|---|
| Dose (ppm) | Positive Animals | Total Animals |
| 0 | 0/68 | |
| 50 | 0/64* | |
| 250 | 4/67 | |
| 500 | 7/67 | |
| 2500 | 13/74 | |
| 6000 | 14/72 | |
| 10,000 | 7/69 | |

* Later data reported one positive at this dose

The most common models used to fit such data are:

1. The Probit Model - which assumes a normal (Gaussian) distribution of sensitivities in the exposed population to the material tested, usually against the logarithm of the dose.

2. The Logit Model - which assumes a response mechanism similar to first order chemical kinetics with a damping effect at upper response levels as "receptor sites," (places on, or in, the cell where the reaction takes place), etc., are used up or become occupied.

3. The "Hitness" Model - including the one-hit and multi-hit models assume that an effect occurs when a vulnerable portion of the cell receives n hits, n being some integer, from 1. Some multi-hit models have been used to describe the rapid increase with age of cancer incidence in man [1]. The assumption is made that n assaults on the cell are necessary to begin the irreversible changes that later show themselves as clinical cancer. The one-hit model is often used in describing the dose-response for radiation effects.

4. The Extreme-value Model - attempts to describe rare events such as the number of floods that will exceed a given height during some long time interval. In a limiting form, the extreme-value model becomes the one-hit model and is, in fact, a generalized "hitness" model without the constraint that the n be an integer.

The major difference among these models lies in the estimated effects at the very low doses in which we are interested. The doses necessary to achieve low response levels (i.e. $10^{-8}$) are substantially different depending on the model used.

The different extrapolations that would arise from the Haltoni data (including data reported after the New York Academy of Sciences meeting,

May 10-11, 1974) assuming several of these models are shown in Table 1. For the logit model a slope of 2.303 (in logarithms to the base 10) was chosen because this corresponds to the one-hit model. A slope 50% larger (3.454) was also used to show the large effect of change in slope. Figure 1 shows these comparisons. Table 2 shows estimated response rates at doses lower than those used in the Maltoni experiment.

(INSERT TABLES 1 & 2 HERE)

The results shown in Tables 1 and 2 are of considerable consequence in establishing "safe" levels or in estimating responses at any suggested levels of exposure. Thus, for the Sprague-Dawley rats, exposed for 1 year, 5 times a week, 7 hours a day (Maltoni's experiment BT-1) at 50 ppm, we would expect as an upper limit, any where from 085 positives out of 100 animals exposed to 2.3 positives out of 100 animals exposed, depending on the dose-response model chosen. At 1 ppm this range (per 100 animals) is .0024 to .047, again depending on the model chosen. These estimates, of course, are [illegible] Sprague-Dawley rats. What this implies for men, exposed different [illegible] different time periods, probably exposed to other co-carcinogens, etc. is not obvious. A conservative view is that genetically heterogenous man is at least as sensitive as the S-D rat, and these estimates should be looked upon as minimum risks to man.

The other class of models is concerned with time to response. Using them to estimate safe doses is based on the obvious fact that everyone must die of something at some time and a new cause of death is important only if it will occur early enough in the lifespan to shorten life. A letter in SCIENCE [2] summed up the arguments this way, "...the only relevant parameter in such discussions is how the average lifespan of a person within a given population may be affected by...exposure. How can...'extra deaths' per year...

be translated into reduced lifespan?"

In the data reported so far by Maltoni and others, information about time to appearance of the tumors and time to death of the animals has not been reported, so these "latent period" or "time-to-response" models are not applicable here. When Maltoni reports tumor deaths observed up to 130 or 135 weeks this does not mean that all tumors appeared only at the very end of the experiment.

There are difficulties with both classes of models for low dose effects. In the mid-range of doses where the experiments are usually done, the data are usually adequately fit by any one of the yes-no models. An example constructed by Cornfield [3] shows how similar the three major models are over a 256-fold range of doses. If given perfect data, we can't tell these models apart in the 2 to 98% range of response, this says that the data you can get often tells you too little about the data you can't get, i.e. you still won't know with certainty what model to use.

MEGA-MOUSE MANIPULATIONS

Under these circumstances it would seem reasonable to attempt to conduct experiments in the dose-range in which we <u>are</u> interested and where the usual models give widely different answers. This has led to suggestions for the mega-mouse experiment. The experiment will have to be mega-mouse to be capable of detecting low levels of damage (say of the order of 1 in $10^6$) and/or small reduction in survival, etc. To demonstrate, at a single dose level, that the response rate is less than 1 in a million, with say 95% confidence and with no spontaneous tumors in untreated animals, would require three million animals each in both a treatment and control group. For a carcinogenesis experiment these animals would have to be maintained on the appropriate regimens for a life-time (about 18 months to 2 years for mice). Obviously millions of animals cannot be started on experiments all at once, so the

experiments would have to be conducted sequentially with great care that animals are appropriately randomized and identified at each stage of the separate subexperiments and that appropriate controls are set up at each subexperiment, etc. To make certain that one had sufficiently sensitive animals it probably would be necessary to set up (relatively small) parallel positive controls -- animals treated with known carcinogens at suitable doses, to show that the experiment was biologically capable of detecting materials at least as carcinogenic as known carcinogens. The numbers added would not be great, but added precautions have to be taken when known carcinogens are being handled. If we take into account that the untreated animals may develop spontaneous tumors, then to detect an increase of 1 in $10^6$ over the spontaneous incidence could require a study several thousand times larger than one in which there were no spontaneous tumors.

Even with unlimited funds to conduct these experiments, the probability that they could be conducted with no mistakes in handling, feeding, loss of animals or any other of the myriad of common laboratory errors that ruin the best planned experiments of mice by men, is very low. Purely logistical problems might guarantee failure. Such laboratory errors, considered as noise, could tend to overwhelm any signal present in the data, making it still more difficult to differentiate between treated and control animals. The statistical remedy is to enlarge the experiment by yet another large factor increasing the risk of further blunders that could wipe put the gains of the increased experiment size. In this kind of experiment if one wanted to show "safety" of a material, quite possibly unconscious pressures would exist to do a poor job. The more errors made, the less likely it is to show a difference

between treated and controls, between signal and noise. Finally, at low dose levels results may be ambiguous, with confusion possible between spontaneous and induced tumors. Thus, we think the mega-mouse experiment is liable to end in a ditch. It does not have as much to commend it on second thought as it looked to have at first.

IF NOT MEGA-MOUSE, THEN WHAT?

In view of these problems, what are the prospects that the low dose experiments proposed by the Manufacturing Chemists Association at the New York Academy meeting will provide useful information? We have computed, for Professor Maltoni's BT-1 data, that a dose as low as 1 part per million is almost certain to have a risk of less than 1-2 in 10,000. What could an experiment at a dose of 1 PPM using several hundred animals show? Hardly anything? We would urge the MCA people to review their design plans. If they cannot design a potentially more productive practical experiment perhaps they should abandon the whole thing.

Difficulties arise in applying any mathematical model at very low doses. Does the slope of the response curve in the mid-dose range hold for very low doses? Is the slope likely to become steeper or shallower at very low doses? If steeper, then any dose suggested as "safe" will be even safer than we think. On the other hand if the slope is shallower, then any "safe" dose will be less safe than we think. Armitage [4] showed that at high doses the curves flattened out -- that there seemed to be highly resistant animals. Is there symmetry in the dose-response relationship? If there is then we should look for flattening at the low end of the response curve, too. Mantel, Heston and Gurian [5] seem to have showed this.

MANTEL-BRYAN EXTRAPOLATION

Nathan Mantel has suggested that in view of these many problems in extrapolation it might be useful, in attempting to compute a safe dose, to fix upon one of the models for which there seems to be adequate experience and a good biological basis, and to fix upon some suitably shallow slope, and with appropriate 95% or 99% upper limit of response calculations, extrapolate to a level which can be agreed upon as a "virtually safe" level. This approach is embodied in the Mantel-Bryan procedure [6] and in recent modifications [7].

Mantel and Bryan suggest using the log probit model, with a slope of 1 probit per 10-fold dilution. Both have been criticized. With respect to the model Richard Peto [8], among others, has suggested that it has little biological basis and that in the field in which most work has been done at low dose levels -- radiation carcinogenesis -- a one-hit model is appropriately conservative [9]. Some of Peto's own work recently would imply that a 2-hit model would fit the data better. Such a model is less conservative than the probit with slope = 1. The criticism of the M-B choice of slope runs in both directions. There are workers who think it is too shallow. A recent review of about 180 papers in the carcinogenesis dose-response literature by the Franklin Institute [10] has turned up many examples of shallower slopes implying that a slope of .1 is too steep.

LATENT PERIOD MODELS

The models involving time to response, need more development. Most of them are concerned with mean or median times to appearance of cancers while clearly what we need is the time for 1% or 0.1% (or some smaller number perhaps) to develop cancer. If this event didn't occur until a late age then the risk,

however looked at, would obviously be small. Gail [11] has pointed out that with one particular model of the distribution of time to appearance, a cancer with a median age of appearance (if there were no other causes of death) of 300 years (e.g. lung cancer) would nonetheless reduce life span for those developing it by about 8 years.

There is also a psychological problem in working with these models, that perhaps someday will be overcome. It's the problem of dealing with an unfamiliar currency. Is something which costs 72 rials expensive or cheap? If you are an Iranian you will have little trouble working this out, but if you're an American tourist you will have to do some translating. How important is a cause of death which shortens average lifespan at birth by 20 minutes, or 2 months, or 2 years? How do you translate that into your own experience? As an aid, or as the first line in the tourist's phrase book, please notice that all cancer, the second leading cause of death in the United States, reduces lifespan at birth, by less than 2 years.

The time-to-appearance models are not free of model assumptions. The Albert-Altschuler model assumes a log-normal distribution of occurrence times. Gehan [12] has shown that this model implies unusual biological behavior with a non-monotone hazard rate. The model that Peto and Pike and their colleagues prefer is the so-called Weibul model which is much better behaved, and does conform better to what is currently known about the biology.

In addition the models developed so far are what the statistician calls "fitting" or "graduation" models. They fit or graduate the observed data, but it is not clear whether they can be extrapolated safely far outside

the observable range; they do not incorporate a "guarantee" that the response will be below a certain level. The Mantel-Bryan procedure does attempt to produce such a "guarantee."

The latent period models have not only inherent experimental (observational) problems but also some unsolved mathematical problems. It's not hard to observe superficial tumors in experimental animals, but what is the time-to-appearance of an internal tumor that kills the animal? That doesn't kill the animal? Do we have to develop experiments with serial sacrifice, designed into them? Again Richard Peto [13] has some suggestions on how to handle some of these data.

Gail points out one further difficulty that the time-to-appearance models have brought more vividly to our attention. These are the "competing risk" problems. Suppose a material can lead to death from any one of a group of causes -- not just cancer. If this material shortens life, so that all the exposed individuals (animals or humans) die early before cancer is likely to occur it may even look like a cancer preventive. This is in the class of the cartoonist, Webster's, advice on how to keep from growing old -- walk in front of a bus. More statistical sophistication is needed to handle the problem of competing risks. With yes-no models survival data as well as the simple "yes-no" response must be considered. Did the animals live long enough to develop cancer? Or, was the material so effective in eliminating all other causes of death that all animals died of cancer at a very late age?

When first looked at it appears that there are large differences in concept between yes-no models and the time-to-appearance models. However, Hoel and Chand [14] have shown how they are related. The Albert-Altschuler models, using a log-

normal time to appearance of tumors correspond to the Mantel-Bryan choice of the probit model where observations would be made at one instant in time for experimental animals exposed to different doses. Similarly the Weibul-based models, favored by Peto and Pike correspond to the "hitness" models, when animals are all sacrificed at one time, and observed for presence or absence of tumors.

MORE TROUBLES

No matter the model used, there still remain a substantial group of unsolved problems. One is the problem of interactions of materials. Beginning with the early initiator-promoter studies of Berenblum [15], research workers have been aware that materials affect each others' effects and often do not operate in an "independence vacuum." Richard Doll [16] has shown that in two important environmental exposures, asbestos and radon (in the exposed uranium miners), the interaction with cigarette smoking was multiplicative rather than additive. This is a frightening prospect which implies that the problems that follow the addition of new materials to man's environment may be much more serious than just adding another drop to the pool. Some work has been done on allowing for the "natural" incidence of tumors in control groups but there is not agreement on the appropriate procedure to use -- simple subtraction, the Abbott's correction, or a slightly more complicated "functional" method proposed by Albert and Altschuler [17]. From the experimentalist's point of view the most unfortunate effect of natural tumor incidence is that it substantially increases the experiment sizes needed to show differences between the treated and control groups.

Then there are questions of dose. Should an animal experiment be a lifetime feeding experiment? A series of pulsed-doses, with zero exposure in between? An exposure for a short time, followed by no further exposure? Exposure in utero? Exposure only relatively late in life? Each of these is meaningful and could have a counterpart in human exposure. How one extrapolates from one to the other is now known.

ESTABLISHING ACCEPTABLE RISK LEVELS

Applying the extrapolations from almost any model will entail problems and sometimes hardship. When people talk about levels they "can live with" they must be reminded that these could be levels that other people might die from. We therefore recommended that the appropriate "safe" level (i.e. a risk of 1 in a billion, or 1 in a million, etc.) be chosen after considering the following:

(a) Is the material already in the environment? If so, how extensively is it used? What are its economic uses? Its health uses? (i.e. is it a medicine for use in a very serious condition? a mild condition? a self-limiting condition?).

(b) Is it a new material? What will it be used for? What are its economic uses? Its health uses?

For example, with materials now in the environment and of substantial economic importance, limiting risk of $1x10^{-6}$, reducing in subsequent years to $1x10^{-7}$ and then to $1x10^{-8}$ may be appropriate. For new materials not yet in the environment, the limiting risk could be set at $1x10^{-8}$, unless there are overwhelming health or economic reasons to indicate higher risk levels. The setting of a limiting risk level should be an "open market" operation.

In the early application of the arithmetic of the models, consideration can be given to how many persons are or will be, exposed to the material. If there are limited numbers of persons exposed to the material, as an initial "safe" level, possibly a risk level as high as $1x10^{-5}$ may be permitted. This level will then have to be progressively reduced to a country-wide or world-wide, universal lower risk. This means a first risk of $1x10^{-5}$ for those "exposed," and perhaps $1x10^{-10}$ for those apparently "unexposed," (but who may even be exposed to a "rub-off" level much as the non-smoking person may be exposed to the smoke from someone else's cigarette). This proposal involves a double standard and raises serious ethical issues as to whether some portions of the population should be assigned higher risk -- suffer the losses -- so that other lower risk portions of the population might gather the gains -- another "open-market" question.

Finally, ways are needed to include non-experimental evidence in setting up safe doses. For example, if man has been exposed to a material for a long time (over 30 years is a long time) and no untoward irreversible effects seen, a way is needed to incorporate these data into the arithmetic. No objective procedures now exist for doing this. Perhaps, as an interim measure until objective procedures are developed, experts could be called upon to modify the "safe" dose. This might be done by a change in the allowable risk level, i.e. a change from $10^{-8}$ to $10^{-6}$. Perhaps the experts should be restricted in making changes in the risk level to no more than 100-fold, i.e. from $10^{-8}$ to $10^{-6}$.

OUT-MOUSE EXTRAPOLATION

After the in-mouse extrapolation problem comes extrapolation from mouse to man - the out-mouse problem. David Rall [18], in a recent symposium

on Statistics and the Environment, at the National Academy of Sciences, dealt with some of the issues very well. We will not attempt here to do more than summarize parts of his discussion, in place using Rall's own language. He points out the difficulties in extrapolating "from an inbred mouse strain to a genetically heterogeneous population, such as man." It appears reasonable (to us) that an inbred strain is likely to have a steeper dose-response curve than would a more heterogeneous population. Rall asks, "If a heterogeneous population is a collection of inbred strains, each with its own dose-response curve, what then would the dose-response curve be for this heterogeneous population?"

Rall also speaks of problems of relative size of the experimental animals and man which lead him to recommend that doses are more likely transferrable on the basis of relative surface area (or 2/3 power of weight) than on a mg/kg basis. He notes the differences in metabolic rates, and in the ratio of blood volume to circulation time which would lead to materials being retained by man relatively longer than they are retained by the smaller experimental animals. If this is true, then equivalent doses of carcinogens could be more carcinogenic for man than for the mouse. Rall also raised questions of plasma protein and tissue binding with the remark that small mammals tend to bind compounds less extensively than man. Because hepatic metabolism is often of major consequence Rall notes that "in general, small mammals metabolize compounds more rapidly than large ones; in general herbivores metabolize compounds more rapidly than carnivores ...The entire area of metabolic disposition of foreign compounds is of major importance."

The generation time of cells, their rates of repair processes, etc., obviously will affect malignant or mutagenic change. "In the mouse...the generation time of the rapidly proliferating cell population is about half of that in man, so that a cancer in a mouse is likely to appear earlier in a mouse's life span than in a man's." This observation has considerable importance with respect to the time-to-appearance models.



We must recognize that experimental animals usually live in a controlled environment, with relatively uniform diets, temperature, humidity, exposure to other agents, etc. Man, as a free living animal, has a much more diversified experience -- some of which will make some of him more sensitive, more susceptible and more likely to succumb to environmental assaults. Some experimenters have argued that the appropriate experimental animal would be a non-inbred animal. Using non-inbred animals reduces the reproducibility of experiments, requiring larger experiments to give answers with assurance. Another suggestion is to conduct experiments in several species using inbred animals of each species and using results in the most sensitive of the species to extrapolate to man.

In spite of all these difficulties, it still seems possible to extrapolate from mouse to man -- at least from the median mouse to some hypothetical median man. To allow for responses of the non-median man, for the more sensitive individuals of the species, will require introducing additional factors. It is less than reasonable to take a no-effect level in a relatively small animal experiment, (for the kinds of effects we are considering here, 100 animals at a dose is a small experiment) and translate it to a TLV or some similar "safe" standard.

COST-BENEFIT, OR WHOSE OX IS GORED?

The remaining issues considered here are ones in which the statisticians have no special competence. On the other hand there's nothing in their training to make them more than normally incompetent, so we think we can talk about these issues, as well (or as badly) as other scientists. These issues are the ones usually lumped together under the heading of "cost-benefit," or, in less elegant language "whose ox is gored?" There were some direct references to this in the N.Y. Academy mtg. when Mr. Mazzocchi asserted that issues of safety would have to be resolved by adversary proceedings. This disturbed some people who then proposed the alternative to adversary activity, cooperation between science, industry and the labor unions.

It seems to us that we really have no alternative to the adversary-type activities when different people have different interests. The scientist who believes that he can resolve all through the use of his science alone impresses us as being out of touch. Does this mean that no cooperation is in order? Of course not. As statisticians, we could not work without the data on who was exposed, how much he was exposed to, and for how long he was exposed. These data must come from industry. To follow-up exposed people we need data from industry and union and government sources. Evaluating animal results, requires cooperation with our laboratory science colleagues. But cooperation does not mean suspension of critical faculties, or suspension of scientific disbelief. If our laboratory colleague has designed a non-productive experiment, we must tell him and try to help him design one that will yield something. If we have misinterpreted or misused data, somebody must tell us. (Usually somebody does.) And the telling

need not be too gentlemanly, either. We would urge saying a lot of these things out in the open where other people can see and hear, too, because these "other people" have a stake in all this - their lives, possibly. We don't find it too dreadful that two letters discussing an industrial exposure to a carcinogen in a recent NEW ENGLAND JOURNAL OF MEDICINE [19] read like exchanges of "you're an expletive deleted." Some good might come of the exchange.



As for "whose ox is gored", we have already referred to the ethical issue of choosing some people to be at risk so that some others (or "Society") might benefit. We believe a good shibboleth in cost-benefit discussions might consist of the Cornfield questions: "Cost to whom? Benefit to whom?" The decisions on the balancing must be made with affected parties included no matter how hard it is to do. It's enough to sit in on a hearing on the possible banning of a pesticide and to see the Department of Agriculture on one side, and the Department of Health, Education and Welfare on the other to know that "The Government" is not a monolith and cannot make the decision, either.

SUMMARY

Where does this all leave us?

It leaves us able to develop rather good animal data at dose levels that don't really interest us. That's a first-class highway that takes us where we don't want to go. It leaves us unlikely to be able to develop good data at "realistic" doses. To extrapolate animal results to man exposed at these "realistic" doses today requires assuming a mathematical model of dose-response in the animal, and conservative use of this model. Then we have to jump from one species to another in ignorance of the terrain of the landing site, i.e. the many species differences. However, we will have

knowledge of some important species similarities and that makes the jump a lot less dangerous. With respect to costs and benefits we are just beginning to understand some of the implications of the arithmetic. We have begun to see that there are few, if any, good ways of totalling the costs or computing the benefits [20]. Cost-benefit may turn out to be another blind alley.

Tomorrow and the next day we must do the appropriate research on species differences in metabolism, in the mathematics of the modelling and extrapolation -- as a minimum. The socially-related issues of what is an acceptable risk; what are the costs; what are the benefits must be discussed in the open, freely. This implies recognizing that someone's costs may be someone else's benefits. (My medical costs are my physician's scurce of living.) The inputs to the cost-benefit algebra are not well worked out. Our ways of working must include the adversary approach as well as the pleasanter way of cooperation. And today, we must get to precautionary decisions for man's safety and health based on the road maps from animal data -- inadequate as they are..

* * * * * * * * * * *

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TABLE 1

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EXTRAPOLATED 'SAFE' DOSE LEVEL (PPB) USING

MALTONI'S LIVER ANGIOSARCOMA DATA*

(99% ASSURANCE LEVEL)

| Extrapolation Model | RISK LEVEL $10^{-5}$ | $10^{-6}$ | $10^{-7}$ | $10^{-8}$ | None Specified |
|---|---|---|---|---|---|
| Probit (Slope = 1, Mantel-Bryan) | 251 (225) | 81.6 (73.0) | 29.2 (26.1) | 11.3 (10.1) | |
| Logit (Slope = 3.454) | 574 (553) | 124 (119) | 26.7 (25.7) | 5.74 (5.53) | |
| Logit (Slope = 2.303) and "One-Hit" | 23 (21.4) | 2.3 (2.14) | 0.23 (0.214) | 0.023 (0.0214) | |
| "Classical" | -- | -- | -- | -- | 500 (not possible) |
| Weil | -- | -- | -- | -- | 125-50 (25-10) |

* The data as of 130 weeks of observation up through dose level 500 ppm, but not higher, were used for extrapolations since the response curve flattened out at higher levels. The numbers in parenthesis show "safe" levels computed from data developed after 135 weeks of observation, which included 1 liver angiosarcoma at a dose of 50 ppm.

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TABLE 2

ESTIMATED RESPONSE RATES: LIVER ANGIOSARCOMA 1/

(99% UPPER CONFIDENCE LIMIT IN PARENTHESIS)

| MODEL | DOSE (PPM) 50 | 25 | 5 | 1 |
|---|---|---|---|---|
| Probit (Slope = 1) | .012 (.028) | .0055 (.013) | .00059 (.0018) | .000041 (.00015) |
| Logit (Slope = 3.454) | .0041 (.0035) | .0015 (.0030) | .00013 (.00027) | .000012 (.000024) |
| Logit (Slope = 2.303) and "One-Hit" | .012 (.023) | .0061 (.012) | .0012 (.0023) | .00025- (.00047) |

1/ Based on data from Maltoni, experiment BT-1, 52 weeks of exposure and 135 weeks of observation

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EDUCATION:

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| 1935-1939 | City College of New York; B.S. in Mathematics and Statistics. Received 1939. |
| 1940-1942 | Graduate School, U.S. Department of Agriculture, Washington, D. C. |
| 1944-1946 | Graduate (ranked first in a class of 57) of U.S. Air Forces Statistical Control School, Harvard Graduate School of Business. |
| 1947-1948 | Graduate study at Ohio State University (Economics and Statistics), U.S. Department of Agriculture. |
| 1948-1953 | American University; M.A. in Statistics. Received 1953. |
| 1953-1961 | American University; Ph.D. in Statistics. Received 1961. (Thesis: "A Family of Truncated Sequential Plans for Normally Distributed Variable"). |
| 1959-1960 | London School of Hygiene and Tropical Medicine, London, England. |

EMPLOYMENT:

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| Feb. 1939-Apr. 1940 | Office boy to production clerk, National Container Corp., Long Island, New York. |
| Apr. 1940-Feb. 1942 | Clerk to Section Chief to Junior Statistician, U.S. Bureau of the Census, Washington, D. C. |
| Feb. 1942-Apr. 1943 | Statistician, Office of the Quartermaster General, U.S. Armed Forces, Washington, D. C. |
| Apr. 1943-Apr. 1946 | Private to 1st Lieutenant (Statistical Control Officer), U.S. Air Force. |
| Apr. 1946-Apr. 1948 | Statistician, Air Material Command, U.S. Air Force, Wright Field, Dayton, Ohio. Also, part-time Instructor, Quality Control Statistics, Wright Field Branch of the Air University. |
| Apr. 1948-Sept. 1948 | Statistician, Strategic Air Command, U.S. Air Force, Andrews Field, Washington, D. C. |
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| June 1955-Sept. 1959 | Mathematical Statistician and Acting Chief, Therapeutic Trials Section, National Cancer Institute, Bethesda, Maryland. |
| Sept. 1959-Sept. 1960 | Rockefeller Public Service Fellow, Statistical Research Unit of the British Medical Research Council, London School of Hygiene and Tropical Medicine, London, England. |
| Sept. 1960-Oct. 1970 | Associate Chief, Biometry Branch, National Cancer Institute, Bethesda, Maryland. |

EMPLOYMENT (Continued):

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| October 1970 -- | Associate Director for Field Studies and Statistics, Division of Cancer Cause & Prevention, NCI, NIH, Bethesda, Md. 20014 |

SOCIETIES:

Institute of Mathematical Statistics
The Royal Statistical Society (Fellow)
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ADVISORY GROUPS, COMMISSIONS, ETC.:

| | |
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| 1963 | Member, Advisory Board, Research Support Center, Veterans Administration Hospital, Washington, D. C. |
| 1972 -- | Member, Task Force on Aging Populations, NCI |
| 1972 -- | Member, Cancer Center Advisory Committee, Howard University, Washington, D. C. |
| 1972 -- | Councillor-at-Large of the Society for Occupational and Environmental Health |
| 1972-1976 | Associate Editor, CANCER RESEARCH |
| 1973-1976 | Chairman-Executive Secretary of the Committee of Presidents of Statistical Societies (COPSS) |
| 1972-1976 | Member, Council for Analysis and Projections, ACS |
| 1973-1976 | Member, Diagnostic Research Adv. Group, NCI |
| 1974 -- | Associate Member of the Graduate Faculty, Georgetown University, Washington, D.C. |
| 1974 -- | Consultative Panel on Hazards of Chemical Pesticides, NAS/NRC |
| 1972-1974 | Member, Board of Directors, ASA |
| 1972-1974 | Member, Executive Committee of the Biopharmaceutical Subsection, Biometric Society |

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| 1958-1959 | Member, American Statistical Assoc. Council |
| 1957-1959 | Member, New York Academy of Sciences |
| 1959 | Chairman, Biometric Section, ASA |
| 1961-1965 | Member, Hematology Subcommittee, BEAR (Cmte. on Biologic Effects of Atomic Radiation, National Academy of Sciences, NRC.) |
| 1961-1965 | Member, Board of Scientific Advisors, Consumers Union, Mount Vernon, New York |
| 1961-1969 | Member, Board of Editorial Advisors, BLOOD, The Journal of Hematology |
| 1962 | Member, Committee on Planning and Information, Assembly of Scientists, NCI |
| 1962-1964 | Associate Editor, Journal of the National Cancer Institute |
| 1962-1968 | Member, Biostatistics Fellowship Review Committee, NIH |
| 1963-1964 | Chairman, Methodology Section, Washington Chapter of the ASA |
| 1963-1964 | Member, Ad Hoc Committee on Survival of Red Blood Cells, NAS |
| 1963-1965 | Member, Diagnosis and Treatment Contracts Review Committee, NCI. |
| 1963-1965 | Member, Drug Evaluation Committee, NCI |
| 1964 | Member, United States-Japan Cooperative Science Program |
| 1964-1970 | Member, Regional Council, Eastern North American Region, Biometric Society |
| 1964 | Member, Advisory Committee on Mathematics Biological Engineering, Veterans Administration Hospital Center, Washington, D. C. |
| 1965 | Member, Ad Hoc Committee on Research Methodology for Use in the Development of Anti-Radiation Agents, Life Sciences Research Office, FASEB |
| 1965 | Member, Nominating Committee, ASA Biometrics Section offices |
| 1965-1968 | Associate Editor; CANCER RESEARCH |
| 1966 | Chairman, Travel Fellowships Awards Committee, Biometric Society |
| 1966-1967 | Member, Feasibility Committee for Preoperative Irradiation on Rectal Cancer |
| 1966-1968 | Member, Chemotherapy Contract Review Cmte., NCI |
| 1966-1968 | Member, the American Therapeutic Society |
| 1967 | Member, Program Cmte., Biometric Society (ENAR) Spring Meeting, Atlanta, Georgia |
| 1967 | Member, Nominating Committee, Assembly of Scientists, NCI |

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| 1967-1968 | Chairman, Subcommittee on Medical Biostatistics, Cmte. on Quantitative Methodology & Drug Developments, American Therapeutic Society |
| 1967-1968 | Member, Study Group, Training Grants and Fellowships, NCI |
| 1968 | Member, Nominating Committee for 1969-71 Council |
| 1968 | Member, Ad Hoc Primary Review Panel, Urokinase-Pulmonary Embolism Trial, NHI/NIH |
| 1968-1969 | Member, Syllabus Committee, Georgetown University School of Medicine |
| 1968-1972 | Chairman, Animal Data and Human Studies, Subgroup IV of the Tobacco Working Group, Lung Cancer Task Force, NCI |
| 1969 | Member, Ad Hoc Working Group on Education and Training, Education & Training Cmte., NCI |
| 1969-1971 | Member, Ad Hoc Cmte., Adv. Cmte. to the Federal Radiation Council, Study of Uranium Miners, NAS/NRC |
| 1969-1971 | Member, Ad Hoc Cmte. on the Evaluation of Low Levels of Environmental Chemical Carcinogens, DHEW |
| 1969-1970 | Member, Advisory Panel on Carcinogenicity of Pesticides, Secretary's Commission on Pesticides and their Relationship to Environmental Health |
| 1969-1971 | Member, Immunology-Epidemiology (IE) Segment, Special Virus Cancer Program (SVCP), National Cancer Institute |
| 1970-1971 | Member, Technical Assistance Committee of the Metropolitan Washington Regional Medical Program |
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| 1971-1973 | Member, International Council, International Biometric Society |
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HONORS & OTHER SPECIAL SCIENTIFIC RECOGNITIONS:

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| 1939 | Phi Beta Kappa |
| 1959-60 | Rockefeller Public Service Fellow (London School of Hygiene and Tropical Medicine) |
| 1963 | Honorary Fellow, Amer. Statistical Association |
| 1968 | DHEW Superior Service Award |
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| 1974 | DHEW Distinguished Service Award |
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TEACHING POSITIONS HELD:

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| 1951 | Instructor in Statistics, Correspondence Graduate School, U.S. Department of Agriculture, Washington, D. C. |
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MR. KLEIN: Your Honor, if I may make a suggestion, our next witness is Doctor Hyatt, and he will address himself to respirators, which in large measure are unrelated to the matters which have been raised by Doctors Kraybill and Schneiderman, and if I may suggest, I would like to open up questioning to Doctors Kraybill and Schneiderman at this time.

JUDGE HYATT: All right. We will make that modification then.

We will proceed, when we open up the questioning of the witnesses of any particular panel, we will first proceed by allowing the Solicitor to commence the questioning, and then questions from the audience.

Do you have any questions?

MR. KLEIN: I have just a few, Your Honor.

To what extent, if any, can we rely on rat responses to vinyl chloride in order to prognosticate the reaction of man to vinyl chloride?

That is for either of you gentlemen. I guess it is for Doctor Kraybill.

DOCTOR KRAYBILL: In many instances We have to go to the rodent as a member of the mammalian system because it is unethical and improper of course to use man for my experiments.

Some people have inadvertently been exposed to agents, and on these we can draw epidemiological conclusions. I think Doctor Schneiderman covered the subject very ably when

he talked about extrapolating from mouse or rat to man; there is always that possibility in there of a species variation, but usually, as I said earlier, when you get a response in the mouse and in the rat, and then confirm it in man, that puts a high index of credibility on the findings as far as a particular agent.

MR. KLEIN: Do you consider human exposure to vinyl chloride at 50 parts per million to be a serious hazard with respect to angiosarcoma?

DOCTOR KRAYBILL: I believe I said earlier that there is a high probability here of it being a serious hazard. Unfortunately, it would be nice if we could go to the epidemiologists such as Doctor Schneiderman and say:

> "We have such and such exposure levels and these are the incidence of the angiosarcoma or angiomas in man."

So I will answer you to say that it is a high, high probability of a cause-and-effect relationship there.

MR. KLEIN: I have nothing further at this time, Your Honor.

JUDGE MYATT: All right. I am going to ask that when I point you out and you have questions for members of the panel, that you come to the microphone and identify yourself before asking your question.

MR. BELICZKY: My name is Lou Beliczky; I am Director

of Industrial Hygiene for the United Rubber Workers International Union. I have a question of Doctor Schneiderman.

I have had a chance to look at one of your letters to John F. Seiberling, signed by you and data done by Doctor Brown, which relates to parts per billion , and if we transpose numbers we come out with numbers something like liver tumors only, .3 of a part per million, and one in one hundred thousand.

I have tried to get information before as to -- if you extrapolated this data just a little bit further than that, what would be the risk at 50 parts per million?

DOCTOR SCHNEIDERMAN: The numbers that have been referred to were computations based on still slightly earlier data from Professor Melton's, and you'll notice the remark was made that at 1 in 100,000 the so-called safe level was roughly of the order of 300 parts per billion; the later data reduced that to 251 parts per billion.

So these are certainly very much in the same ballpark.

To extrapolate these to the level of 50 parts per million, or -- that then is 50,000 parts per billion, 50,000 compared to 250 -- that would bring me, if this particular relationship held, to the level of risks of the order of less than one in a hundred. Excuse me; risks greater than one in a hundred.

And I think this is of the order of risk that Doctor Kraybill mentioned when he said we could have a five percent risk -- that is five in one hundred -- of workers exposed at that level.

JUDGE HYATT: All right. Yes, sir?

MR. TOPOL: My name is Allen Topol and I am representing Tenneco Chemicals, Inc., and I would like to ask Doctor Kraybill, first, sir, what is the latency period for angiosarcoma of the liver?

DOCTOR KRAYBILL: I gave you some figures a while ago; I don't know how firm these are in man, and they range anywhere from, I suppose the figures are accurate -- their data is accurate when they first thought they got the exposure, until the time that it was actually diagnosed by the Commission -- ranged anywhere in these 19 cases from about 11 to 30 years.

MR. TOPOL: Does it generally range over such a wide period of time? For cancer in man?

DOCTOR KRAYBILL: Yes. That can vary, and I think it was pretty ably discussed earlier.

When you are referring to genetic variations -- we have such a thing as pharmacogenetics, and people respond differently to different agents, and we see this in animals also, this variation from strain to strain, or species to species.

MR. TOPOL: Well, focusing on the cases developed

among employees in the United States in polyvinyl chloride plants, there have been 13 such cases. Is that correct?

DOCTOR KRAYBILL: Well, I have reported here, and I think someone said earlier, according to this sheet, there are about 19 cases of liver angiosarcoma.

MR. TOPOL: Well, in terms of the American cases; I think these are the worldwide.

DOCTOR KRAYBILL: All right. Let's subtract six; that's right. 19.

MR. TOPOL: And how many polyvinyl chloride plants are there in this country which are 20 years or older?

DOCTOR KRAYBILL: That I have no idea.

MR. TOPOL: Well, there are eight plants, and let's accept that, and I want to ask you a question based on that.

If employee exposure to vinyl chloride was the critical ingredient that caused the angiosarcoma, then wouldn't you expect the number of cases of angiosarcoma that have been detected to have been reasonably divided among the plants 20 years or older?

DOCTOR KRAYBILL: That, I think, will depend on a search on how good the epidemiology is from plant to plant, and the Goodrich Plant came in with their data; I don't know how good the statistical epidemiological survey is on all the other plants around the country. That is what it is based on.

It goes back to an old statement; they talk about a

toxic agent and a stress, and they said:

"You don't see an effect here, a chronic effect."

and this is a chronic effect, and you can only see a chronic effect, or chronic toxic effect unless you look for it.

It depends on how well you look, and how good the epidemiological survey is and the search.

MR. TOPOL: Well, assuming that the epidemiology was reasonably equal from plant to plant, in point of fact, we ended up here with seven cases in a single plant, and with five other plants 20 years or older having no cases at all.

I mean, what sort of probability would you attach to that, assuming the vinyl chloride was the causative factor?

DOCTOR KRAYBILL: Well, there could be here a variation in the controls and the exposure levels t hat one is getting. I saw some figures on the TLV for vinyl chloride where they talked about levels of 160 parts per million to 600 parts per million.

I have heard the figures bandied about of 1,500 to 2,000 and some values above that.

So it is just like in your animal experimentation; your incidence, or your response, is going to be directly related to the exposure level, and the higher the exposure the more cases you should get and perhaps also it should shorten the induction period. Conversely, the lower you go

on the dose, the longer the induction period, and the fewer number of cases that will arise.

MR. TOPOL: Well then, if I understand you, Doctor Kraybill, are you saying then that one possible explanation for this phenomenon is that exposure limits -- I'm sorry; exposure levels at the plants at which the employees had cases were significantly higher than the vinyl chloride exposure limits at other plants?

DOCTOR KRAYBILL: I don't know that. I can only guess, and many of us have, that in the years past, that the exposure levels were perhaps higher for vinyl chloride, and with time, with the innovations in our industrial hygiene and our controls, I would think the industry had attempted to button things up and get better control on the exposure.

But the thing about it is that years ago, if they had a high exposure, the hideous thing about it is that even if there is a cessation in exposure -- and with the induction period of 15 to 20 years, that could very well fulminate, or come into full bloom later on.

MR. TOPOL: But now we are considering only the plants that are 20 years or older, and the fact that seven cases showed up in one plant and five plants in that 20 years or older, operating at an earlier period, had no cases, and my question to you is: isn't one possible explanation for that the fact that levels of exposure were higher in the one plant

that had the cases than in the others 20-year-and-older that had no cases.

DOCTOR KRAYBILL: I can only guess, , and in a way I kind of agree with you. I can only guess on that.

MR. TOPOL: If you reach that judgment, at least tentatively, isn't it possible then that only at levels of exposure of the high levels that existed in that one plant at that time, that that is what is required to induce the angio arcomas in humans, and that when you move to lower levels you don't find the cases, as a matter of fact?

DOCTOR KRAYBILL: I wish I knew the answer to that. As I said earlier, that is an epidemiological proposition here, and we don't have monitoring data.

I don't think the industry, unless they can parade it forth, as I said earlier -- you have to have good monitoring data to make these predictions; just as I said in the animal experiment, you have to equate a dose against a response, and you need monitoring data to make some speculations on this.

MR. TOPOL: But what you are saying is that if you knew that there were levels in other plants, to which employees were subjected to approximately equal to the one in the plant where the angiosarcoma was induced, you would be led to the conclusion that there was some other agent, at

least partially responsible, wouldn't you, for the angiosarcoma?

DOCTOR KRAYBILL: I said that in my remarks. We have not completely ruled out the possibility that there are ancillary compounds here -- associated contaminants. That is always a possibility, and that has to be ferreted out by further experimental work.

There is always a possibility that a contaminant or interactant may enhance a particular response.

MR. TOPOL: In other words, you are saying that there may have been a different agent working, that if that agent had not been there the angiosarcoma would not have developed?

DOCTOR KRAYBILL: That is a good hypothesis. We don't know.

MR. TOPOL: I just don't know at this point now in time.

DOCTOR SCHNEIDERMAN: May I, Mr. Topol, comment on some of these things you have been talking about?

MR. TOPOL: Surely.

DOCTOR SCHNEIDERMAN: It seems to me that you are raising the standard interesting questions concerning the effects of agents in which not every one -- or even a very small proportion of individuals are common to the agents. A more common one that you and I are far better acquainted with than vinyl chloride is cigarettes.

With high levels of cigarette smoking, nonetheless, only -- and that is a very peculiar "only" that I am saying -- only about 20 percent of the very heavy smokers will die of lung cancer.

Nonetheless, there are some people who are rather light smokers who will die of lung cancer. What are the other elements that go to contribute toward this particular response in human beings?

Doctor Kraybill has indicated at least one of them. There are some genetic differences; there are certainly differences in additional things to which people are exposed.

There is fairly substantial evidence that in some industrial exposures there are multiplicative effects, of different agents of exposure. For example, what Richard Dahl has reported with respect to the asbestos workers who smoke as opposed to the asbestos workers who do not smoke.

Finally, with respect to your question about a probability, I am going to give you a somewhat snide answer with your question about what is the probability that an event has occurred?

The probability is one. It has occurred.

Do you want to know, with all these if's and caveats that you have created, what is the probability if all other things were equal, thatsome other things would be unequal? I think you are now -- excuse me for saying this, but

you are in the realm of fairyland.

You couldn't demonstrate that all these other things were equal that you talked about; you built an if upon another if upon another if upon another if, and when you got finished with it, Doctor Kraybill called this a guess, and you dignified it by calling it a judgment.

I think you have really -- I see what you are pursuing, but I must say you have carried us way away from the existing data.

MR. TOPOL: Well, let me say that with regard to obviously the question of whether or not the assumptions are valid would depend on the record.

Let me ask Doctor Kraybill a different question from his testimony, if I may, sir.

You discussed in the beginning of your testimony the dose response curves, I think when you were discussing animal experimentation.

Isn't there sort of a disagreement among scientists as to whether these dose-response curves go through zero in all cases, or don't? I mean, or restated, at least among some scientists, isn't there a view that there is a threshold safe level for exposure to a chemical carcinogen?

DOCTOR KRAYBILL: I think Doctor Schneiderman covered that pretty comprehensively earlier, when he talks about a steep slope and a shallow slope, where the curve gets

asymptotic, so to speak, to the abscissa, and when it gets asymptotic or gets a shallow curve, then you are getting down into low insult or low stress area, and here is where you have to magnify or focus your experiment on larger numbers of animals to titrate this effect.

I think this is a statistical epidemiological type question you are asking me, and I think it should be answered by a statistician.

MR. TOPOL: Well, I -- okay; Doctor Schneiderman, if you would.

The question really is that does the curve always intersect zero, or are there safe levels at very low threshold levels, for chemical carcinogens, or is the science such that we don't know the answer to that important question?

I mean, I am talking now in fact, not theoretical calculations.

DOCTOR SCHNEIDERMAN. Yes. In fact, the answer is that we don't know.

MR. TOPOL. Okay.

Let me ask you, Doctor Kraybill, a different question about the animal experimentation that you discussed.

None of that work was done in NCI, where you are, right? The basic work was the Viola, the Maltoni and the Industrial Biotest? Right?

DOCTOR KRAYBILL: That is correct.

MR. TOPOL: As far as the Vida work, the highest exposure that Viola subjected his animals to was 30,000 ppm; correct?

DOCTOR KRAYBILL: That is correct.

MR. TOPOL: And as far as the Torkelson and Rowe -- you did not mention them; didn't they also do some work on animal testing of rats and mice that was published in 1961?

DOCTOR KRAYBILL: I didn't mention their work, but this goes back to some earlier toxicity work on VC.

MR. TOPOL: And didn't Torkelson and Rowe conclude in their 1961 paper that exposure to vinyl chloride at concentrations of 50 parts per million failed to induce tumors in rats, hamsters, rabbits and dogs?

DOCTOR KRAYBILL: I am not familiar with that report.

MR. TOPOL: But to the extent it did, and I would like to offer it for the record, then that will obviously speak if it contradicts the later work that has been done by Maltoni and ECI. That will speak for itself, I gather.

JUDGE WYATT: Mr. Topol, let me interrupt you at this point. Now, I notice that Tenneco is scheduled to make a presentation; is that correct?

MR. TOPOL: Yes, Your Honor; that is correct.

JUDGE WYATT: You can offer it at that point. At this point we are interested in questions, and I am afraid

perhaps I am going to have to move in on you a little bit, because you're sort of monopolizing the floor, and I think some others might want to ask some questions.

How many more do you have?

MR. TOPOL: Just a couple of additional questions, if I may.

JUDGE MYATT: As lengthy as the prior questions?

MR. TOPOL: No. I will try to keep them brief.

JUDGE MYATT: I would appreciate that.

MR. TOPOL: Thank you.

Insofar as the industrial biotests are concerned, isn't it a fact that the lowest level of exposure at which any angiosarcoma have been observed in that test is 50 parts per million?

DOCTOR KRAYBILL: That is correct.

MR. TOPOL: And wouldn't the same be true for dalkoni?

DOCTOR KRAYBILL: That is correct. We got it also in rats and mice.

MR. TOPOL: So that when we go to the level below 50 parts per million, we are really making theoretical calculations as to whether angiosarcomas would or would not be induced at those lower levels; isn't that a fair statement?

DOCTOR KRAYBILL: I think I said that. That is a speculation, but the thing about it, as I pointed out, that

this is only in six months, and people have been quoting this as two animals in 200, and I have received the admonition from Doctor Calandrew that that is not quite correct, and these animals can go to 12 months with additional exposure.

So I say, I speculate that one might expect a higher incidence here. I am sure NCA will report on these studies later, because now I think that would be about nine months down the pike, so they may have additional data.

MR. TOPOL: One final area, very quickly.

What is the point of the Government research going on at Pine Bluff, Arkansas, having to do with carcinogenesis? What is the point of that? Isn't it to determine to what extent or whether safe levels exist for some chemical carcinogens?

DOCTOR KRAYBILL: They are interested in that effect at the low-dose level, with many, many animals, but I understand that they are going to perhaps testify here, are they, at this hearing? They are not?

Well that is what they are interested in, that part of the -- the shallow part of the dose-response curve where you receive a low insult.

MR. TOPOL: In other words, this is a large-scale Government research to determine what the safe level is for various chemical carcinogens?

DOCTOR SCHNEIDERMAN. If there is a safe level.

DOCTOR KRAYBILL: Yes, if there is a safe level.

I would like to state something here. I have this reference now, by Torkelson, Owen and Rowe, and it is in the Industrial Hygiene Reference Book, reported that repeated seven-hour exposures for six months at 200 parts per million resulted in histological changes in the central labular regions of the liver of rabbits.

Of course, they didn't get it in rats, guinea pigs and dogs, but they did get some liver effects, some liver damage.

MR. TOPOL. Well, I think that -- as I said, we will offer this later. Thank you.

JUDGE HYATT: This gentleman right here.

MR. BECKMAN: My name is Jerome H. Beckman, and I am General Counsel for the Society of the Plastics Industry.

Doctor Kraybill, I would just like to inquire as to whether you are familiar with the publication "Food and Cosmetics Toxicology," widely read, I think, by toxicologists?

DOCTOR KRAYBILL: Yes, sir, I am.

MR. BECKMAN: You testified earlier, if I am not mistaken, that -- and I am not sure I'll pronounce these names right, so I'd appreciate your correcting me -- that -- would you mind repeating the names of the other two known causes of angiosarcoma in the environment?

AMD-25

DOCTOR KRAYBILL: I think I talked about thorotrast inducing --

MR. BECKMAN. Thorotrast and arsenic pesticides; is that correct?

DOCTOR KRAYBILL. That's right.

MR BECKMAN: Are you familiar with an article that appeared in the publication I mentioned entitled "Induction of Liver and Lung Tumors in Rats by the Simultaneous Administration of Sodium Nitrite and morphaline."?

DOCTOR KRAYBILL: No, I am not.

MR. BECKMAN: Well, I might direct your attention to that. That publication indicates that in Sprague-Doiley rats these chemicals also cause angiosarcomas of the liver.

Another article I might direct your attention to and inquire about, in case you are familiar with it, is one on "Neoplasms in the Rat Associated with Administration of Eurathan and Alfatoxin."

This article was by Newburn, Hunt and Logan, and appeared in Environmental and Molecular Pathology." I think that is another well-known journal.

DOCTOR KRAYBILL: That one I would be more familiar with, because I have worked in the field of aflatoxin, and aflatoxin is almost -- I'd say almost comparable to vinyl chloride, because it is a potent hepatocarcinogen, but aflatoxin interestingly enough attacks the hepatocites, and pro-

duces a hepatoma.

Vinyl chloride, until this recent wire that we got from Maltoni, indicated that it was strictly on the endothelial cells, but now he says probably a hepatoma. I think that makes vinyl chloride an interesting thing as far as the site of action.

There are other chemicals, yes, sir, there are other chemicals. I believe the hydrazines have been implicated also, in producing experimentally angiosarcomas.

MR. BECKLEY. The only reason I asked that question, obviously, is that for example, sodium nitrite and other chemicals are more ubiquitous in the environment in many ways than the arsenical pesticides, and the other one that I can't pronounce.

Is that not correct?

DOCTOR KRAYBILL. Yes, than morpholine.

This doesn't take us off the hook, because we are working on that problem, too. We are very much interested in nitrosamines also, because that is a general population type of exposure.

MR. BECKLEY: I realize that and I just wanted the record to show that there are other materials that can lead to this effect.

Thank you very much.

JUDGE HYATT. All right; anyone else?

MR. NORD. Doctor Schneiderman, my name is Peter J. Nord; I am an Industrial Hygienist with the Amalgamated Clothing Workers of America.

Doctor Schneiderman, in the paper by Torkelson and Rowe thatwas referred to a few minutes ago, I believe the animals were -- most of them were sacrificed after six months; a few were held for up to two months longer.

Do you consider this length of time -- six to eight months -- an adequate length of time for determining the carcinogenicity of a chemical?

DOCTOR SCHNEIDERMAN. I am glad you gave me that additional information, because I was wondering how, with those dose levels, those animals survived long enough for anything to happen.

You know, remember the old cartoonist, Webster, who used to have a cartoon called "How to Keep from Growing Old," and one of his -- every once in a while you'd get some advice on how to keep from growing old, and one of them was to walk in front of a streetcar.

I think how to keep from developing cancer is to die of something sooner, and with these very high dose levels, I would suspect that most of those animals were long gone before the cancer could develop.

JUDGE MYATT: Yes, sir?

[VOICE.] I would like to direct this question to either Doctor Schneiderman or Doctor Kraybill.

Do you feel, from your knowledge of the biotest studies that there were sufficient numbers and species of animals exposed in the exposure schedule and the concentration of VC was adequate enough to predict a human response in VC?

DOCTOR KRAYBILL: I understand -- and again, I believe ICA is going to comment on this later -- but I think that lower doses are indicated in their experimental work. So that should give us a better handle on the dose response relationship.

VOICE. My question for a statistician, I guess, would be, were there sufficient numbers of mice or rats examined in either the Maltoni or the biotest studies to make a proper analysis?

DOCTOR KRAYBILL. Let me say something, and Doctor Schneiderman, I am sure, will want to comment on this, too.

That in the first work of Maltoni, where they were using 60 animals, this was one of the criticisms that was made, and since then we have gone to 200 to 300 animals. Obviously, if one would go to 500 to 1,000, that would give you a better index, or confidence limit, I guess you call it, as to the credibility of your data; the higher number of animals you go, you can titrate in to get a better handle on the incidence figure.

But certainly, with the few numbers of animals, you

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may miss. I am not/statistician, but with the fewer number of animals, you may miss a tumor, whereas if you extend the number of animals you may pick it up then.]

[DOCTOR SCHNEIDERMAN: I don't know the biotest materials, so I can't comment on them.] I have heard reports on them, but I haven't seen them so I can't comment on them.

[But in general, with respect to any experiment in carcinogenesis, the larger the experiment, the better it is done, the higher the dose levels at which the materials are given, the higher will be the doses of the so-called safe doses by these computational procedures that I gave you.

So that the computation of safe levels takes into account the experiment size. The experiment is trivial, then the safe level will be trivial. If the experiment is very small, the safe level will be extremely low.

If the experiment is very large, and no effect has been seen at/very large dose level, then the so-called safe dose that we compute from that will be very close to that level at which this large experiment was conducted.]

So all experiments, in this sense -- all experiments if well conducted -- that is, if there aren't sloppinesses in the laberator/ -- are valid with respect to their size. It is that the small ones contribute a little, and the large ones contribute a lot.

[VOICE. Is it not a fact that Maltoni's study

and his mice and rats were relatively small in numbers? 268
Certainly under 100?

I see you nodding your head in the affirmative, Doctor Kraybill; is that correct?

DOCTOR KRAYBILL: Yes, it was, and he went to a greater number of animals in his later work, and that may be a plus value. That may be a plus feature.

VOICE. Have either of you gentlemen had the opportunity to examine anything other than the telegram that Doctor Maltoni sent?

DOCTOR SCHNEIDERMAN. Yes. I have been given tabulations and other material other than the telegram, and my computations did not include the material listed in the telegram. Mine were data presented earlier by Professor Maltoni at a meeting of the New York Academy of Sciences.

By the way, in the computations that we do, we do not use the information only at a single dose level. Maltoni did experiments, including controls and up to one, two, three, four, five -- seven dose levels, at roughly 70 animals -- 64, 68, times seven -- roughly 500 animals.

So the data that went into the -- contributed to the numbers that I produced, are based on not quite all 500 animals, but/a substantially larger number than 70, the number you mentioned for the single dose level.

VOICE. Are you saying that your statistical

analyses would have been ultimately more valid if there had been a higher number of animals examined and studied?

DOCTOR SCHNEIDERMAN. NO. My analyses are valid no matter what number I use.]

Let me just say again, how you should pay attention to the experiment size and what the numbers are.

If larger experiments were conducted, and we got, let us say, in these larger experiments, very low levels of response, then the numbers that we would compute as parts per million and parts per billion for safe levels, would be higher.

The smaller the experiment, the lower will be the numbers that are computed as safe levels My statistical computations take into account this experiment size thing that appears to be concerning you.

[VOICE: Have you had an opportunity to examine a statistical analysis of the people that have died, and the people that have been exposed to polyvinyl chloride in the industry, to determine -- is there any merit to determine that an extrapolation between the studies of Maltoni and humans are valid?

DOCTOR SCHNEIDERMAN. I have not looked in detail at the human data which you talk about. The extrapolations are related to several things. Extrapolations derived from theoretical concepts, what the dose response

curve is, they derive from theoretical concepts -- how is a man like a mouse, how is the rat like a man, and in addition, I would hope, as someone who is concerned with the problem of cancer and the problem of preventing it, that I would hope that in the future we need not have cases in man to demonstrate that some material might be a potential risk to man.

So if what you ask would be done, I don't find it necessary, other people might.

VOICE: Do you have any evidence that suggests that any level below 50 is capable of producing a malignancy of any kind in any species?

DOCTOR SCHNEIDERMAN. Yes. The evidence -- if I fit these data with the dose response curve, and I fit them with any one of the acceptable dose response curves, there are levels below 50 which this dose response curve says to me will produce these tumors.

The world does not come to an end; 50 is not a cliff. If I have a dose response curve that is going like this, I don't fall off the cliff at 50. It will continue.

There is a nice thing about nature; there is some continuity in smoothness, and things of that sort. That is what I am depending on, by the way; I am depending on the continuity of nature.

VOICE. I understand you spoke at the meeting in

New York on May 11. Were you present when Dr. Maltoni gave his presentation?

DR. SCHNEIDERMAN: Yes, sir.

VOICE: Were you present when he was asked whether or not an extrapolation between mine and humans, in terms of exposure, produced a comparable time period when it came to over-all -- I guess the death of a human versus the death of mice; and his answer was that in his opinion if the mice had died at 50 parts per million, it was somewhere between 70 and 80 years of experience for a human being?

DR. SCHNEIDERMAN: I don't recall this. I must have been dozing at that time.

VOICE: Okay. Thank you.

JUDGE MYATT: Are there any further questions? There's a gentleman over there on my right.

MR. FLEMING: My name is Fleming; I am with Air Products and Chemicals; I have a question for Dr. Schneiderman.

Dr. Schneiderman, I believe that all of the statistics you gave and the theoretical studies that you made were based upon experiments on Sprague-Doiley rats made by Dr. Maltoni; is that correct?

DR. SCHNEIDERMAN: Yes. I refer to his BT-1 experiments done on Sprague-Doiley rats.

MR. FLEMING: Now, it is my impression, sir, that Maltoni also did some work using Whistar rats. Are you familiar with those experiments?

DR. SCHNEIDERMAN: Maltoni reported in New York that he had started to experiment with Whistar rats; these experiments are not as far along in their observations as the ones with the Sprague-Doiley rats, and the level and nature of exposure was different, and the level of response was lower.

MR. FLEMING: The level of response was lower, I

gather that means that if you repeated your computations based on the Wistar rats, you would get an entirely different set of figures and these would be much higher? Is that correct?

DOCTOR SCHNEIDERMAN: I would like to wait until these animals have been observed long enough -- you know, for the 110 weeks, like the other animals have been observed.

If no more tumors developed in these Wistar rats, yes I would get higher levels.

MR. FLEMING. Well, based on the data currently available that would you project the result would be?

DOCTOR SCHNEIDERMAN. I think I indicated my preference on that and see what the data are. Let Jean Dixon do the crystal-balling.

MR. FLEMING: I am sorry, I guess I had the impression you were going quite a bit of that here, today.

JUDGE MYATT: Yes, sir?

MR. GARING. My name is Garing, and I am with the Dow Chemical Company, and I would like to address this question to Doctor Schneiderman.

You said that the expected incidence at 50 parts per million, in reference to -- or in answer to a previous question, was greater than one percent.

I would like to ask, how much greater than one percent? Five percent, seven percent? Ten percent?

I so, would you project this to still higher levels of 100 parts per million, 200 parts per million,

500 parts per million, and 1,000 parts per million and enter that in the record, please?

DOCTOR SCHNEIDERMAN: I don't think I can answer you accurately in how much greater than one percent. I did some pencil and paper calculations here in terms of the extrapolations I had down to one part -- a risk of one positive event in 100,000, and I will do the calculations that you asked, and I will have them entered into the record.

But, as I said, I did them in pencil and paper here, and like so many statisticians, I really can't do arithmetic very well.

JUDGE STAUT: Are there any further questions?

I note that we are getting near 12.00 o'clock, but I would like to get to Doctor Hyatt before we adjourn for lunch. So we will take a very, very brief -- I'm sorry, there is another question.

After this question we will take a very brief recess and then resume Hyatt.

MR. GHELCH: My name is John Ghelch, New England Plastics.

Are there any differences in the functions of the livers of the animals tested and human beings?

DOCTOR KRAYBILL: Differences in the functions of the livers in human beings?

MR. GHELCH: Versus the animals tested.

DR. KRAYBILL: That can depend on many variants. It could depend

on the role of the diet, the genetics, the insults, the drugs that are taken, and all these sort of factors.

MR. GELCH. There are approximately 20 or 30 tests for human liver functions?

DOCTOR KRAYBILL: Yes.

MR. GELCH. If those tests were performed on the animals that were subjected to VCM, would they have similar liver functions? Would they show those functions?

DOCTOR KRAYBILL. Oh, I see what you are getting at.

They may or may not; about six or seven years ago there was a very elegant symposium held in this very area, called 'Comparative Pharmacology,' and they have, in this instance, across various animals with different agents, going the whole way from the frog right on up through rodent to man himself and the monkey, and each one of these has shown a slight variation when you are talking about liver enzymes, like SGOT, LDH and SGPT and that sort of thing.

If again goes back to an earlier remark I made about pharmacogenetics, too.

But there are variations from species to species and there are variations perhaps in strains.

MR. GELCH. In the case of the rats that were tested, there is only a minor variation or are there some major functions? Are you saying that there are only minor variations in the --

DOCTOR KRAYBILL: I haven't seen any clinical data on this. The only thing we have seen is the tumor data. You are talking about biochemical lesions and biochemical effects now.

MR. GIELOW. I am talking about basic liver functions.

DOCTOR KRAYBILL: Yes, you are talking about liver function tests, as I said -- SGOT, bilirubin and things of that sort, and also the enzymes which reflect this.

I haven't seen any of that data in the animals.

MR. GIELOW: What you are saying is you don't know if they are quite similar or if they are quite dissimilar?

DOCTOR KRAYBILL: I would suspect there might be a slight variation among the species and among the strains.

MR. GIELOW. What is the incidence of angisarcoma of the liver in human beings? The incidence in the population? It is listed in the press as a rare liver disorder.

DOCTOR KRAYBILL: That's right; it is about one in 900,000.

DOCTOR SCHNEIDERMAN. I think I can talk to that.

We have just completed a survey called the Third National Cancer Survey, in which we tabulated the incidence of new cancers in a roughly ten percent population in the United States, over a period of three years.

In this ten percent sample over a three-year period,

we had eight angiosarcomas of the liver reported to us.

I don't know your definition of rare, but that it qualifies for me.

MR. GHELCH. I don't know the definition of rare; that is why I asked.

DOCTOR SCHNEIDERMAN: Right.

MR. GHELCH: And if you eliminated those deaths that were related to working in vinyl chloride plants, how would that number change? Would it be reduced by one or two? Or significantly reduced?

DOCTOR SCHNEIDERMAN: This is now being looked into, to how many of these were vinyl chloride, polyvinyl chloride related. I don't know it.

MR. GHELCH: Based on a response in the rats tested of 50 parts per million, what would you feel would be the equivalent response level in the human being? Taking into account all the things that you mentioned -- body weight, rate of metabolism, volume of the blood in the body, area of the lungs and things like this?

Do you have a basic relationship?

DOCTOR SCHNEIDERMAN: That is essentially the same question Mr. Gehring asked when he said would I care to estimate how much greater than one percent the risk would be at 50 parts per mil[illegible] and as I said, I will do the computations on this. I will submit them to the record.

Let me remark that my computations are -- carry with them the following statement.

I will sort of guarantee you that the risk will be less than whatever the stated risk is. I am stating an upper risk, I guarantee it will be less than that. And like all guarantees, it may not hold

[DR. GELCH.] I just would like to clarify that, and that is my last question.

I am not clear on your answer. My question was: if you had a 50 parts per million response level in a rat, is there any way that you can reasonably estimate if that 50 parts per million will elicit the same response in human beings, or will it be at a higher level?

I am not trying to badger you up on levels, but what I am saying -- I am not trying to say, you know, that the cliff existed at 50 parts per million, but what I am saying is, [is 50 parts per million the same response level in human beings? OR, recognizing the difference in metabolism and size and everything else, is it a higher or lower level?

DOCTOR SCHNEIDERMAN: I would be amazed if they were the same. Whether it will be higher or lower, I don't know; I would suspect, in terms of industrial exposures that since the rats were exposed for -- what? -- 52 weeks, which I would guess is roughly about a 30-year working life

span, and were exposed seven hours a day, five days a week, I would hope that the response rate to men who worked in these factories would be less, since by and large, most people don't work at the same particular operation for 30 years. I would think that they got somewhat of a lower level of exposure.

You get -- when talking about this you begin to get into issues of -- is it level of exposures, are there peaks of exposures? Is a peak exposure -- is a level twice as high for half the time as bad as a level every day at half the high level?

These are issues that are not resolved. I hate to be so indefinite and vague about it, but that is as definite as I can be. But that's my current knowledge.

MR. GILLCH: Let me come in the back door.

If a 50 parts per million level was an efficacious level in a rat, what would the efficacious level for that drug, whether it be VCM or what, be in human beings? Would he be able to take -- or, generally do you find that the response that you are getting in the rat is a fraction or a multiple of the response level that you get in human beings?

DOCTOR SCHNEIDERMAN: When we were looking at drugs, and we were looking to see what were efficacious levels in humans, we would work toward levels that produced a given

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amount -- these are anti-cancer drugs, so you can work with fairly toxic things. You would work with drugs that produce a toxic level, kill ten percent of the rats or mice that we're working on.

We would then take that level and drop it down substantially before we gave it to a human, perhaps cut it by as much -- anywhere from a sixth to a hundredth, before we started working on it, and then very cautiously increase that level so the general impression that at least the physicians treating cancer patients have -- now, this is in a different area, because you raised this.

MR. GMELCH: It is a good area.

DR. SCHNEIDERMAN: The general impression that physicians treating cancer patients have is that man may be more sensitive than any of the experimental animals, and therefore we ought to start at least trying out these drugs with even positive action at substantially lower levels, so that we don't have the overwhelming toxicity in man.

MR. GMELCH: All right. Thank you very much.

JUDGE HYATT: All right; we are going to take a very, very brief recess.

Before we do, Dr. Kraybill has made another submission, and so, to clarify the record, Mr. Reporter, the first submission, which is marked Exhibit 10, will be 10-A; the subsequent submission will be 10-B.

[Exhibit 10-B marked.]

[Brief recess.]

JUDGE HYATT: Dr. Hyatt.

DR. HYATT: Relative to my qualifications on respiratory protective devices, one aspect of my employment was as Alternate Group Leader of the Industrial Hygiene Group at the Los Alamos Scientific Laboratory from 1949 to June 30 of '71. I was then Leader of the Respirator Research and Development Section until July 1, 1973, the time of my

retirement. I am now self-employed, an industrial hygiene consultant, residence Los Alamos, New Mexico.

I have served as a member of the Joint AIHA ACGIH Respirator Committee, was editor and contributing author to the Respiratory Protective Devices Manual.

I believe it is worthwhile to note that a lot of the work relating to respirator testing and evaluation that I have participated in and conducted since 1956 has been under the auspices of the AEC at the Los Alamos Scientific Laboratory, and in -- July 1, 1971 the NIOSH funded an extensive respirator research and development program at the Los Alamos Scientific Laboratory.

As a result of the work sponsored by NIOSH, some of the results were to develop respirator man-test systems that would quantitatively measure the efficiency of various types of face pieces, to develop quality control test methods. These methods and systems have been developed and delivered to the NIOSH testing and certification lab in Morgantown, West Virginia, for the last two years.

I further would like to note that I was not involved in the recommendations of respirators in the vinyl chloride standard. I reviewed this in the past ten days, and I have been asked to give some basic comments relative to the evaluation of the respirators recommended in the standard -- how effective are they against vinyl chloride, how practical are

they [illegible] work in, how long can one work in these devices, and the availability and cost of such devices.

Also, I will conclude by making recommendations for respirators for protection against vinyl chloride. These will be based on approved devices that are available.

I would first comment on Section C of the standard, and it is noted that the continuous flow and pressure-demand type of respirators are proposed based on NIOSH recommendations. It is further noted that NIOSH has observed leakage through [illegible] chemical cartridge respirators at high concentrations.

This has been verified by Nelson and Harter at the Lawrence Livermore Laboratory; they have tested approved cartridges against several hundred solvents. They have tested vinyl chloride at a concentration of 1,000 parts per million, at a flow rate of 53 liters a minute, and they find a breakthrough of one percent in 3.8 minutes.

They dropped their test concentrations to 125 parts per million, too, then found a breakthrough of one percent in ten to twelve minutes. The volume of the sorbent was 140 to 150 milliliters.

This is the type used in the small chemical cartridge respirators.

The industrial size gas mask was not tested by Nelson; this contains at least -- generally a thousand milliliters of sorbent.

I note this to the further verification that the available, approved, organic vapor chemical cartridge respirators apparently are not satisfactory because of their very short service life.

I would note that the observed leakage is no justification to eliminate a demand type atmosphere-supplying respirator, there was no discussion relative to facepiece leakage in the standard.]

I would note that the test methods and data that we have developed under NIOSH sponsorship are available to test each user, to assure facepiece leakage less than one-tenth percent.

[I would like to comment, under Section G, paragraph 3, relative to the four types of respirators that have been recommended.

The first device is a positive pressure full facepiece, self-contained breathing apparatus. This is equivalent really to the second device described, because it is assumed that -- it is intended to be positive pressure 100 percent of the time in the facepiece by describing a positive pressure full facepiece SCBA.

There are some that think this is a chemical -- a Chemox, for example, a self-generating oxygen mask; our tests have indicated, and others, that the Chemox will not maintain a positive pressure at all times in the facepiece.

At rest, one percent; at very heavy workloads, we have noted as little as only 50 percent of the time is positive pressure. Thus that one should be eliminated, and we go to Number 2.

The standard describes this as a pressure-demand, full facepiece, self-contained breathing apparatus operated in the pressure-demand mode.

This device, of course, is available and would recommend the corrected description of this device, which is an open-circuit, self-contained breathing apparatus in pressure-demand mode, with full facepiece.

The third item recommended is a combination Type C pressure demand full facepiece respirator operating in the pressure-demand mode, and a pressure-demand, self-contained breathing apparatus operating in the pressure-demand mode.

A more simple and, I believe, correct description is simply a combination type-C supplied-air respirator, pressure-demand type, with auxiliary self-contained air supply.

The fourth item recommended, a combination type-C continuous flow respirator in a pressure-demand self-contained breathing apparatus operated in the pressure-demand mode, does not exist.

Perhaps in preparation of this, reference had been made to a publication by a Joint Respirator Committee of the American Industrial Hygiene Association and the ACGIH, which

which was published in 1969, titled, "Conditions for use of airline respirators in atmospheres immediately hazardous to life or health."

I was a member of that Committee, and I think I am guilty, too, of putting in a recommendation which was repeated here that didn't exist. Theoretically it perhaps would be possible.

Now I would like to comment relative to the efficiency of the two devices that do exist and are real, the -- both devices operated in the positive pressure, of course, are capable of providing protection with a leakage less than 0.01 percent.

I would like to note that the two devices are commonly recommended, and of course approved, for atmospheric concentrations immediately dangerous to life. I think it is worth noting for the record that the Bureau of Mines and now the Mine Bureau of Mines approval schedules approves for concentrations immediately dangerous to life a self-contained breathing apparatus, hose-mask with blower, and a gas-mask for concentrations of gaseous contaminants immediately dangerous to life.

Now, I believe I should note that immediately dangerous to life applies most commonly to materials like hydrogen sulphide, for example. Certainly if a man is wearing an atmosphere supplying device, particularly a

supplied-air respirator, if he loses his air supply for any reasons, immediately he would have to jerk it off, and would he lose his life in some concentration immediately dangerous to life?

This has now been applied to materials, perhaps like vinyl chloride, and certainly like Plutonium 239, that have a long-delayed effect. I was a member of the committee that wrote the American National Standards Z-88.2 in which it is noted that very high concentrations of Plutonium may be immediately dangerous to life.

I note this only because this is the basic classification these two devices recommended would normally fall under.

My later recommendations for respirators for protection against vinyl chloride are based on the assumption that one part per million of vinyl chloride is not immediately dangerous to life on a delayed basis, be it five or 30 years.

How practical is it working in these devices? Let us speak first to self-contained breathing apparatus described; there are three devices approved for 30-minute life that fall in the category of self-contained breathing apparatus pressure-demand type with open-circuit.

Two of these devices are available with choice by the wearer to choose between pressure-demand with positive pressure in the facepiece, or demand, which means a negative

pressure in the facepiece.

The other manufacturer has a device that is available only in pressure-demand, because their philosophy is if it is dangerous enough to insist you wear only positive pressure in the facepiece, the wearer should not have the choice.

I note these simply for the record.

These devices, if they were to be used in large numbers, I am told by representatives from industry, would require approximately two years to deliver an adequate number for use in industry, as proposed.

They cost approximately $450, depending on the quantity you buy, et cetera.

The devices, I believe, for routine work, are very impractical. It must be remembered that these are the emergency devices that are used by most fire departments throughout the United States for emergency use.

There have been certain instances, for example, a fire in one of the Atomic Energy plants, in 1970, where they had very high concentrations of Plutonium. They did have to go in and work in self-contained breathing apparatus: they were highly trained, -- they could work only 30 minutes, and would have to come out and spend five to ten minutes to put a new cylinder on, and then they would re-enter to do the work. And all of this with, of course, an impervious

suit over the self-contained breathing apparatus.

The weight, it would be fatiguing. Certainly they weigh from 25 to 35 pounds. The unit, as I indicated, requires extensive training; the Bureau of Mines, of course, has mine-rescue teams, trained, which covers many days of a training course, and they of course use the device approved for two hours, or longer, protection -- not just because the devices described are considered by the Bureau of Mines as auxiliary devices, not for mine rescue, but they do require quite extensive training.

It requires extensive maintenance.

These devices have to be -- and it is recommended, even by the manufacturers, that periodically they be sent in or you establish your own service maintenance. Many places using them extensively, such as San Francisco Fire Department, have their own maintenance men and full-time on this type of work.

I would estimate that they would have very poor worker acceptance with the 30 to 35 pound self-contained breathing apparatus, some will refuse to wear it, some will have claustrophobia. In our tests of 90 firemen, which are test subjects, testing all types of self-contained breathing apparatus -- and these were even trained firemen, when they would put on a device that they were not familiar with, they would panic, they would get claustrophobia.

So I am suggesting perhaps one percent of the people that would be required to wear these simply could not tolerate them, for physiological or psychological reasons.

I have been asked how long they could wear these devices without excessive fatigue. I am not aware of any work in this area that would point out -- well, I would point out that the major interest has been, and my work has always been to encourage or insist that manufacturers come up with respirators that are purifying respirators, of lowered breathing resistance.

Because of the excessive load, the man must do to purify the air, as he breathes through the filter or the chemical sorbent. Great goals have been made in this area. NIOSH has set lower standards in this area, but I would point out that for approval, the types of devices described require 1 to 1.5 inches of positive pressure in the facepiece.

I have made inquiries, and I do not have any good answers from the physiologists as to how much fatigue this would bring on a workman over a long period of time.

There is another area I would like to comment on; this is relative to subsection or Section L, paragraph 4, on maintenance and repair.

This indicates, and I paraphrase, that for mainten-

ance and repair, a whole-body air-supplied suit impervious to vinyl chloride and a respirator specified in Subsection G must be worn.

Now, this really must be a typographical mistake, because you can't wear them both, and I would ask if there was a small difference in philosophy when this was written, because the previous basic four devices recommended in Subsection F were all pressure-demand types with a tank, so if his engine, for any reason -- his air supply was cut off, he wants to be able to escape without an exposure whatsoever.

A continuous flow supplied-air suit, impervious or not, approved, -- is not approved by the Bureau of Mines or NIOSH where protection against concentrations immediately dangerous to life simply because, again, the possibility of failure.

Now then, I think that I would like to conclude by listing my recommendations for respirators for protection against vinyl chloride, but before listing these I would like to note that, based on one part per million of vinyl chloride exposure is not immediately dangerous to life by delayed action.

Also, I would recommend only currently approved and available devices, and based on test results available to me, and those published, relative to sorbents for protection against vinyl chloride, and specifically I am referring

to the devices used in approved chemical cartridge respirators or gas mask. I would not recommend an air-purifying respirator at this time, because I have seen no evidence to indicate it will give adequate service life.

And I might comment -- I read earlier, for example, ten to twelve minute service life -- well, correction; 3.8 minute service life at 1,000 parts per million. I would like to note that all of the organic vapor cartridges tested and approved by the Bureau of Mines, now NIOSH, was tested against 1,000 parts per million of carbon tetrachloride. The service life of this easily sorbed solvent is 77 minutes, as reported by Nelson.

So, all conditions identical, you get 77 minutes, compared to 3.8, which indicates that the service life is not adequate.

Also, based on NIOSH and AEC-supported research at Los Alamos, which I directed up until July 1, '73, on over 4,000 quantitative man tests to determine the face-piece leakage of all types of devices, the results of this indicate, based on face-fit, the half-mask efficiency for all face sizes and shapes was 90 percent.

This would give a protection factor of ten, with a negative pressure in the face-piece. The protection factor is brought up for the first time in my discussion, and I did wish to refer to the standard under Section 5, subparagraph 7,

that does require that vessels to be entered shall first be ventilated and monitored so that the concentration of vinyl chloride is reduced to the level within the protection factor capability of the protective equipment.

I would suggest that if this term is going to be used in the standard, it must be defined. A protection factor is an index of the protection afforded and is defined as a concentration of the ambient air concentration divided by the concentration inside the face-piece of the wearer of a respiratory protective device.

Preceding the half-mask then by the tests indicated, the protection factor of ten, with a negative pressure of the face-piece; and this applies to air purifying, it also applies to a supplied-air respirator operated in the demand mode with the negative in the face-piece.

The full face-mask, which is easier to fit and fits around the periphery of the face, has an over-all efficiency of 90 percent relative to fitting efficiency. This will give you a protection factor of 100 with a negative in the face-piece.]

The usefulness of the protection factor, which is routinely used in the Atomic Energy establishments, for example, a respirator with a protection factor of 100 can be used by a wearer up to 100 times the TLV or the MPC of the given contaminant, and he will only breathe one MPC or one TLV.

This gives an indication of its use.

[All right, with these qualifications the basis of my recommendations, my recommendations are as follows -- and they are broken into three basic categories:

For protection up to 100 parts per million of vinyl chloride; then I will give those for protection up to 1,000 parts per million of vinyl chloride; and then for protection in concentrations greater than 1,000 parts per million of vinyl chloride.

The first category, for protection up to 100 ppm VC, this is assuming the detection limit of one ppm -- one. A type C supplied-air respirator demand type, with full face-piece.

Because of the toxicity of vinyl chloride, I do not think that a half-mask face-piece should be used with a negative pressure. This applies tommy other highly toxic materials, which, if you're interested, later I can give examples. So only full face-piece.

Item 2. A combination type C supplied-air respirator, demand type, with full face-piece and auxiliary self-contained air supply.

Item 3. Open circuit, self-contained breathing apparatus, in demand mode, with full face-piece.

All of these full face-pieces with protection back to 100, therefore they have to be limited to use up to 100 ppm

based on a detection limit of one.

I do not speak, and don't ask me any questions about tolerance, I take what is written in the standard and I make my recommendations thusly. If it is something else, they can always be extrapolated. I am giving mine on the basis of the efficiency tests on the respirators.

Now, the second classification is for protection greater than 1,000 parts per million of vinyl chloride.

One: combination type C supplied-air respirator, pressure demand type, put with full facepiece, with auxiliary self-contained air supply.

Two: Open-circuit, self-contained breathing apparatus in pressure-demand mode, with full facepiece.

Pardon me, Your Honor, I do think I skipped a category.

The first category was for protection up to 100 parts per million, and I was indicating the second one for protection up to 1,000 ppm, and I believe I was reading devices for greater than 1,000 ppm. I apologize, and I will go back and correct:

For protection up to 1,000 ppm of vinyl chloride, the type C supplied-air respirator continuous-flow, with half-mask face-piece, full face-piece helmet or hood. This is a continuous-flow device, with positive pressure at all times.

The third category should have been for protection

greater than 1,000 ppm of vinyl chloride. This has also been interpreted for protection in unknown concentrations for entry into tanks of limited-egress situation. And I did read those; if you missed them, I could read them later.

I would like to note that if a sorbent has been or is developed that effectively sorbs vinyl chloride with an adequate service life, the goal I would look for would be, say, eight hours' service life at 200 parts per million. Then I think that one can consider, as far as our air-purifier respiratory protective devices; such as a full-face gas mask, chin-style, lower back or front-mounted canister with full face-piece.

One could consider a combination type C supplied-air respirator, demand type, pressure-demand or continuous-flow type, with full face-piece and air-purifying sorbent cannister.

I note this because if this respiratory protection is required at all times, there are always work situations where the workman must move from one level, from one station to another, at great distances, and he must disconnect somehow his airline respirator, whether it is positive pressure or whether it is negative pressure, and have protection while he is moving.

The No. 2 device recommended in the standard, of course, contains that auxiliary air tank, with a ten-minute

supply.

Availability of that device has only been, by the one company that has approval on that, a hundred of them made, and it costs about $450, there will be two years' delivery time on that. I note this because of the importance of considering the sorbent if one is available.

A man could still disconnect the airline and breathe through a sorbent, if you had an efficient sorbent, and move to his next work station.

As it is now, he would have to wear pressure-demand, supplied-air respirator, with an air cylinder with only a limited ten-minute supply. This would have to be changed many times during the day.

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I believe one other point I would like to note: If a satisfactory quantitative man-test system would be used by the operators, by the manufacturers, for example, for testing the efficiency of the face fit, that is, leakage under simulated work-condition exercises, to assure leakage less than one-tenth percent, devices with negative pressure and a full face-piece, I believe, could then be used for protection up to 1,000 parts per million of vinyl chloride.

What I am proposing is quite different, and is only used now by many of the AEC contractors, that is, that you don't just run a simple fitting test, which is many steps above what most industries do, to send the man to the tool-

crib and say, Here, Joe, take the respirator and read the instructions in the book.

Hopefully, they read them.

It requires extensive training, which, for example, with the quantitative man-test system which we've been using for many years in our laboratories, a man reports and takes two hours of extensive training, and he tests them all: half-mask face-pieces, full face-pieces -- because you must keep in mind one fact: all face-pieces, be they half-mask or full face-piece, manufactured in the United States are only made in one size.

If you want to try to find a manufacturer with more than one size face-piece, you would have to go outside the United States, and they are not usable because they are not approved in this country.

The work sponsored by NIOSH will, of course, help us catch up, and, I can say, I have worked with them on the proposed amendments to Part 11. This would be eliminated. But what I'm saying now, you could buy all of the face-pieces, set up one of these commercially available, man-test systems and conduct fitting tests, and instead of a protection factor of 100 which has to be assigned to all, individuals with various sizes of faces, various shapes of faces, then you could determine realistically the protection factor.

Thank you.

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JUDGE HYATT: All right.

Mr. Klein, do you have any questions?

MR. KLEIN: I have just a few, Your Honor.

Mr. Hyatt, directing your attention to the size of the face-pieces, do all manufacturers make the same size face-pieces, or would that vary from manufacturer to manufacturer?

MR. HYATT: No, sir, they do not all make the same size. This information was in a paper that I presented in '71, published in AIHA Journal on the respirator efficiency testing with DOP.

We specifically pointed out half-mask face-piece sizes, in fact we compared them, and the only anthra-metric data known and published has been by the Air Force. Air Force oxygen masks. Take the basic, large, medium and small, which is comparable to a half-mask face-piece, fitting over the nose and under the chin. You will see that one size sold is comparable to the large size Air Force oxygen mask. Another one, comparable to the small size.

One, a very good one, is comparable to the medium; and one is quite different than anything else, is quite wide, a half-inch wider than anything made. This would cover a large mouth like mine; when I smile, in some of these masks you can see my teeth. Obviously that would leak.

Each one approaches it differently, and tries to

come out with the best designed face-piece that he will think one size will provide the protection for the largest number of individuals.

MR. KLEIN: Would there be small, medium, and large, full-face and half-face respirator masks available at this time?

MR. HYATT: No, sir, not at this time. This type of information, which NIOSH again has sponsored, the reports are available, research on developing this for the future work, Webb & Associates, for example, in working with Los Alamos; there's been a report published on the proposed test panel.

So that men and women, that is representative of at least 95 percent of the face size and shape of the working population in the U.S.

This is in the future. It is anticipated that this amendment to permit this will be published. Then the manufacturers are going to have to have some time to then design two or more sizes, whatever they think. The current thinking is that they will let them come up with sizes to fit all men, all women, and only 95 percent of those.

MR. KLEIN: Are there respirators that fit well, described as a typical size face, today?

MR. HYATT: There are respirators to fit the typical size face. But there are no tools or ways to select the device in

relation to even measuring the face.

Now, yes, we've got into this, and it's been suggested, the only such use of calipers, for example, to measure a face, is in the Air Force. And it's very important for high-flying aviators that they select the right size face-piece.

And even with those, I'm told by authorities that work on this, there's some three to five percent of them that they have to make custom respirators, at great expense; nothing fits them.

So the average size -- no one yet has defined what is an average, easy-fitting face. I pretty much can pick one out after all these years of fitting them, I know where the trouble comes.

MR. KLEIN: Now, with respect to industry practices today generally, do you know the approximate number of hours that employees have been actually wearing respirators?

MR. HYATT: This varies widely.

MR. KLEIN: Could you give us the range?

MR. HYATT: The obvious answer, first, is that prior to the advent of OSHA, there were not many of them wearing them routinely, when they should have been wearing them; and they really only started to look at some of these places to enforce the wearing of respirators.

One that I'm familiar with and know about, they are

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requiring the use of respirators on all coke [illegible]s at all steel plants. And they require these eight hours a day. These are half-mask air-purifying respirators they are using now.

There is an instance of using them continuously during their entire workday and workweek.

There are instances where men are wearing supplied-air respirators, where they are doing, for example, grinding or cutting on lead, or lead-contaminated material, for long periods of time.

The only way you are going to approach your answer is to pick out certain types of industries, where some of these devices are used, and then each industry is going to vary.

So, are they worn continuously? I really don't have the answer on this, only industry, by each type, and each type of device. You see, I know of no one wearing a self-contained breathing apparatus continuously, except where there has been a major accident. And I noted the incident of the fire, with Plutonium exposure.

The only thing available, and the concentrations were so high that they were immediately dangerous to life, was a self-contained breathing apparatus. They did wear it for many weeks. There was no choice.

But they only wore them about two hours in the

morning and two hours in the afternoon, and they had two crews, for example, to do the work.

MR. KLEIN: Now, in your testimony you indicated that between 100 parts per million and 1,000 parts per million you would recommend a one-half face-piece. But, under 100 parts, you recommend a full face-piece. Could you explain the reason why?

MR. HYATT: Pardon me, if I gave that impression, I sure didn't mean to. I would like to come back and say that -- I must ask you first: Are you referring to air-purifying demand type, with a negative in the face-piece?

I would like to re-emphasize, for any supplied-air respirator, with a negative in the face-piece, in the demand-mode, I would not recommend anything but a full face-piece.

Now, if you're referring to -- and I did say a combination supplied-air respirator, continuous-flow type, with a half-mask, with a full face-piece suit, or hood -- yes, this was in the category of recommending for protection up to 1,000 times.

MR. KLEIN: Yes. Could you -- I glean from that, that you did recommend a half face-piece. Is that right?

MR. HYATT: Yes. On the basis that there is a positive pressure at all times, and unless eye protection is needed from, for example, the atmosphere, a half-mask can be fitted and used with positive pressure, and give as good a

protection as a full face-mask. It is simply not as stable on the face. This is some that those in charge will know which one is adequate and satisfactory for the individual use.

MR. KLEIN: Let's talk about the compressed-air, when you're requiring a continuous-flow --

MR. HYATT: Oh, yes.

MR. KLEIN: Do you have any recommendations with respect to the sources of compressed-air? In other words, would you recommend taking from the ambient air?

MR. HYATT: A very good question. And I did mean to bring that out. There is a requirement, of course, under OSHA's use and regulation respirators, specifying air quality. And this, for example, Grade D air under compressed-gas association standard, G-7. But no place in there does it say anything about vinyl chloride. It limits CO, it limits other materials, but Grade D even allows 20 parts per million of CO, carbon monoxide.

I recommend on a Grade D, and I understand OSHA is considering this, because 10 parts per million I think should be the limit.

Now let's come to air quality. There's two considerations here. One is, first, for supplied-air respirators, whether it is a continuous-flow type or a demand type. And you have to consider, of course, the number of men. It takes

a very large amount of air. There has to be a large compressor -- compressors are available -- with a large holding tank, in case of power failure, that the men will have time to escape.

This is going to create a problem, because that compressor is only going to compress the air which surrounds the compressor. And if you don't have sorbent sufficient enough to use air-purifying respirators, I don't know whether we would be able to purify the air enough without locating it upwind from the plant, at some distance, and I certainly think that the limit of vinyl chloride in compressed air should be less than any limit that is permitted, for example, in the workroom.

And a rough guideline is only -- always been approximately ten percent. If we're looking at one part per million detectable, I'm suggesting, now the air is one-tenth parts per million would be the maximum permitted in breathing air.

The other major category simply is self-contained breathing apparatus, having their tanks full. They can do this with a compressor. This is available from commercial sources, many companies are providing compressed-air, washed-air, or they are making synthetic air from liquid oxygen and nitrogen.

MR. KLEIN: Do you know about the availability of

such services?

MR. HYATT: No, sir, I have not checked into it. I do know that it's available in most parts of the United States. If they were suddenly asked, for example, to provide 10,000 cylinders of compressed air, it might tax some of their facilities.

MR. KLEIN: Again returning to the sizes of face masks. Could an employer obtain a variety of sizes of face-pieces by buying respirators from several suppliers?

MR. HYATT: Yes, sir. That is what I meant to allude to earlier, when -- for example, we've been doing [illegible] testing, and being in a government laboratory [illegible] all sorts of problems of ordering by trade name, and we were ordered by Washington, back in '56, to cease and desist. But we insisted that was the only way to protect the user, to buy each of the commercial devices, and fit the user, because two things are necessary:

One is to provide an adequate fit; the other is to find one that is comfortable: wear acceptance.

At best, any of these devices are an instrument of torture.

MR. KLEIN: Now, again directing your attention to the recommendations that you've made, could you give us some information with respect to the cost and availability of these respiratory devices?

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MR. HYATT: Yes, I have noted this briefly on certain types.

Let's start with the simplest devices, keeping in mind I have not recommended that any air-purifying respirators:

If adequate sorbents were available, a half-mask, chemical-cartridge respirator normally sells in the range of eight and a half to ten dollars, depending on quantity purchased.

A full-face gas mask, industrial size cannister, will sell in the range of $100 and $150 now, I believe. It's very hard to keep up with the prices, the way they are going up.

Supplied-air respirator, demand type, with a half-mask face-piece, you might purchase for 100, 125, you add 30 to 40 dollars if you put a full face-piece on that.

Self-contained breathing apparatus would run $450.

Does that give you an idea of the range?

So, actually, anything I recommended, it sort of starts at 100 to 150 dollars and goes up to at least 450.

MR. KLEIN: In your testimony you indicated that you had an underlying assumption that vinyl chloride was not immediately hazardous to health. If vinyl chloride were immediately hazardous to health, would your recommendation be changed in any way?

MR. RYAN: You mean if some specific concentration, like if -- if the standard was to say that the underlying philosophy of protection, that there must not be a trace of vinyl chloride breathed at any time during the worker's life, certainly that would be immediately dangerous to life, and I really doubt, if there is respiratory protection, that would be used, that is practical, that would mean shutting down the operation.

Or [illegible] to specify.

You see, all of the industrial hygienists recommending respirators are used to working with a number, which is immediately dangerous to life, some concentration. We have nothing here.

[ JUDGE SMITH: Well, assume for a moment that there is a level that would be immediately hazardous to life, whatever that level may be. Would your recommendation above that level be different than, for example, your recommendation at 500, [illegible] 100 ppm, or below 1,000 ppm?

MR. RYAN: Oh, yes, sir, very definitely. ]

I have been serving as a consultant for NIOSH and reviewing some of their proposed criteria documents on recommendations for respiratory protection; and certainly they have dealt with some of the contaminants, where there is a known concentration that is immediately dangerous to life. One has to approach it every time that way.

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Certain devices are safe up to that concentration, sir, and then above that it takes specifically what exists right here in the two devices, which are listed as No. 2 and 3, that are recommended under subsection (g).

JUDGE HYATT: Anything else, Mr. Klein?

MR. KLEIN: Nothing at this time, Your Honor.

JUDGE HYATT: Does anyone from the audience have any questions?

Yes, sir?

MR. KANE: I am William Kane, representing Diamond Shamrock.

Mr. Hyatt, do I understand your testimony correctly that your recommendations are based on the assumption that the maximum vinyl chloride that can be tolerated is one part per million? As proposed in the standard.

MR. HYATT: I start with that, yes, sir. I simply said that I, as an illustration, I was recommending, based on 50 ppm being efficient for a negative in the face-piece, you do up to 100 times the detectable limit of one. If it was five, closely 100 times five.

MR. KANE: But --

MR. HYATT: Until -- there has to be a limit.

MR. KANE: Yes.

MR. HYATT: To come up with that magic number. You get up to 10,000, for example, immediately dangerous to

per million in the face-piece. If one looks directly at the standard, it must -- there must be no detectable level, really I should say it would be less than, and you would put in a safety factor, and you might say up to 90 parts per million instead of 100 -- up to 900.

This is something that judgment and experience would have to look at, and would have to get advice on where you come up with it. Do you see my point?

MR. KANE: All right. I see that point.

Let me just ask you my question, then; and that is, if you change your goal and say that you wanted to protect workers against exposures not in excess of 25 parts per million, what changes would you make in your recommendations of equipment?

When the worker was going to be in a working area where the vinyl chloride was at levels up to 100 parts per million, and when the worker is in an area with exposures up to 1,000 parts per million, and your goal is to insure that he is not exposed, either in a working area or in his face mask, to more than 25 parts per million. Would that change in the fundamental starting point alter the equipment recommendation that you listed in your testimony?

MR. HYATT: To some extent, certainly, that wouldn't change one's recommendations. Part of the problem is that we've been looking in vain to find what the odor thres-

hold is in vinyl chloride. I see it's quite controversial.

A chemical cartridge respirator, as approved now by NIOSH, should never be used against anything where there is no warning to the wearer that the sorbent is used up. This really applies to gas masks, except that it can be controlled. It has such long service life, compared to the small cartridge.

So, what I am saying is it would make a great difference where the odor threshold is, and on that I will not comment; I don't know.

On 25 parts per million? If you can detect it by odor, and if you have good sorbents, you could use a chemical cartridge respirator.

Certainly 25 parts per million implies it is not nearly as toxic.

MR. KANE: Well, I was hoping you might tell us what specific changes you make in your recommendations of the specific equipment that would be appropriate for use. Perhaps you are not able to tell us precisely what changes you made because you haven't studied the problem with that different starting point. I don't know.

MR. HYATT: This is right. I made recommendations based on 99 percent efficient full face-piece, and actually the positive pressure is more efficient, and what I would like to stress: the Joint Respirator Committee, this technical

respirator committee of AIHA, ACGIH, we have been working on this, and I have proposed and written a series of four selection guides in the last three years.

It is very difficult, as you know, in the U.S., to get a consensus standard, or even a guide. We were able to get one last October, with a Respirator Committee of some 16 members. This has been sent to NIOSH, and I believe OSHA has copies of this, and they are coming down to the point.

Supplied-air respirator, positive pressure, we propose an upper limit of protection factor of 2,000, for example, for a continuous flow of supplied-air respirator, with full face-piece; and 1,000 because the eyes are unprotected, even with continuous flow.

My purpose in noting this simply is that you are at a disadvantage, and this has not been published except as an official recommendation from the Respirator Committee, and this was -- I have a copy with me, if anyone is interested in seeing this later, or it may be put in the record. This was officially sent, signed by me and the chairman of our Respirator Committee to Dr. Charles Powell, at NIOSH in Rockville.

JUDGE MYATT: Do you have a copy with you?

MR. MYATT: Yes. It's in my briefcase. If you would like, I will bring this out.

JUDGE MYATT: Please submit it for the record.

MR. KANE: Thank you, Mr. Myatt; that's all I have.

JUDGE MYATT: Are there any other questions?

You would!

Is there anybody else before we get to him?

All right, but let's wait until he gets the document.

Thank you, Mr. Hyatt. This will be put in the record as Exhibit No. 12.

[Document referred to was marked Exhibit No. 12 and received.]

JUDGE MYATT: Proceed.

MR. Mr. Hyatt, how long do you estimate it will take American industry to obtain the six to ten thousand safety packs or space suits that you've recommended?

MR. HYATT: Well, that obviously should be directed towards the manufacturers. Since it has been brought up, and there is considerable interest in this, well, I have discussed it, for example -- I'll be specific -- with Mine Safety Appliance, and they have indicated a two-year delivery time.

But I must stress that they didn't say ten thousand, five thousand, or one thousand; they just said, with the indicated numbers and the size of the industry, delivery time is two years. So I can't answer that.

MR. Okay. Have you talked to any

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other companies, other than Mine Safety Appliances?

MR. HYATT: No, I have not. I have attempted to, in the short time -- I have only known for three days that I was coming here to this hearing; there was an indication a few days earlier, but that really didn't give me time to make these contacts.

MR. Do you have any recommendations as to what would be appropriate in the interim, while we're waiting for the two years to receive these space suits?

You're not certainly suggesting that we go out of business for two years, are you?

MR. HYATT: No, sir. I'm suggesting, and I have made some recommendations even to consider the use of supplied-air respirator, continuous flow,or demand type supplied--air respirators.

These are much more available commercially.

And the other device is the self-contained breathing apparatus, for example.

I have no estimate. These are used by the tens of thousands, compared to maybe a maximum of 10,000 self-contained breathing apparatus now used by the fire departments. This came from an estimate of converting from demand to pressure demand, I am not sure, others may have better figures.

MR. Have you had an opportunity to

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look at the reactors that any of the companies own?

MR. HYATT: No, sir, I have seen no reactors and I have never seen a process, where vinyl chloride is manufactured, processed, or anything else.

MR. You could not then make any comment on the safety factors that might be involved in using a back-pack or a long cord; is that correct?

MR. HYATT: Right. I can only comment, not from firsthand, on what I know the situation is, and what anyone selecting -- and that is that one must very definitely take into account the activities of the wearer and the safety factors. These are -- has to be considered.

MR. Do you think a space suit is practical if an individual employee is going up and down stairs or working long distances away from where the air is supplied?

MR. HYATT: Of course you're going back and forth between self-contained and space suit -- by space suit, I assume you mean a supplied-air suit?

MR. Right.

MR. HYATT: There's some resemblance to a space suit, certainly they are a lot cheaper.

But no, it is not a very practical device, where a man moves great distances, there's no question he has to disconnect.

MR. Do you think it's practical for

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an individual with a pack on his back climbing down into reactors, where a blade is on the bottom of the reactor?

MR. HYATT: It would depend on the situation, I can't give you a simple answer to this, you must go through the whole procedure that is specified. For example, in a respirator manual and other manuals that have been written relative to the man going in with a life-line on him, any situation that has limited egress, it is all spelled out before he ever goes in.

You have to take a look at the situation, it might be a combination unit. I don't know.

MR. One final question.

As I understand it, you have been helping NIOS. with their recommended proposals; is that correct?

MR. HYATT: Yes, NIOSH has asked me to review some of the proposed criteria documents, these sections on respiratory protection. That's right, sir.

MR. Have they made you available to testify for the Department of Labor today?

MR. HYATT: No, sir. Perhaps I should have stressed that I do some consulting for NIOSH, some for AEC, and this is the first for the Department of Labor. I was simply called up here as a consultant, sir. I am self-employed.

JUDGE HYATT: Any other questions?

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Yes, sir?

MR. OELFKE: Mr. Hyatt, I am Carl Oelfke with Dow Chemical.

In your cartridge-type respirator test, I believe you reported 53 liters per minute test on 1,000 parts per million break-through at the first of your talk.

MR. HYATT: That's right, sir.

MR. OELFKE: Is the 53 liters per minut -- is that a standard test for cartridges?

MR. HYATT: No, sir.

The Bureau of Mines, NIOSH, approval schedule specified either 32 LPM or 64 LPM. Both of them are used.

This was chosen, you must remember when Mr. Gary Nelson reported on the research project, and he tested these under simulated breathing grou, pulsating flow versus continuous flow. He found that, on cartridges, there was no difference -- but a heavy workload is equivalent to his use of 53 liters per minute, not 32.

MR. OELFKE: Are you say, then, that the heavy workload of human beings or the breathing rate on a heavy workload of human being is 53 liters per minute?

MR. HYATT: That's what he is proposing, sir. And I have no reason to challenge his data. I have seen enough date, and we have run tests that -- we've made suggestions, and I think NIOSH is considering, for example, whether the flow

rate should be increased from 32 LPM to maybe 40 or 42 LPM.

And proportionately higher for the rapid flow.]

MR. GELFER: Thank you very much.

MR. HYATT: Thank you.

JUDGE HYATT: Any other questions?

Thank you, Mr. Hyatt.

We are going to adjourn for lunch. We will resume at 2:30.

[Whereupon, at 1:35 o'clock, p.m., the hearing was recessed, to reconvene at 2:30 o'clock, p.m., the same day.]

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Exhibit 13

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Exhibit 13

STATEMENT OF
MARCUS M. KEY, M.D.

DIRECTOR
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
CENTER FOR DISEASE CONTROL
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

ON

PROPOSED PERMANENT STANDARD FOR VINYL CHLORIDE

AT THE
OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION HEARING
U.S. DEPARTMENT OF LABOR
BEFORE ADMINISTRATIVE LAW JUDGE
GORDON J. MYATT

JUNE 25, 1974

I am Dr. Marcus M. Key, Director of the National Institute for Occupational Safety and Health, a program of the Center for Disease Control, in the Department of Health, Education, and Welfare. Under the Occupational Safety and Health Act of 1970 we have responsibility to "...develop criteria dealing with toxic materials and harmful physical agents and substances which will describe...exposure levels at which no employee will suffer impaired health or functional capacities or diminished life expectancy as a result of his work experience." The Institute is also authorized to "develop and establish recommended occupational safety and health standards." Because of the urgency of the vinyl chloride (VC) problem, we have not had time to develop formal criteria for exposure to VC although much of what we present today can serve that purpose. We have, however, recommended to the Occupational Safety and Health Administration (OSHA), Department of Labor (DOL), a recommended work practices standard with environmental monitoring and medical monitoring, and these have served as the basis for the presently proposed OSHA permanent standard for occupational exposure to VC developed under Section 6(b) of the Act. It should be noted that my memorandum of March 11, 1974, transmitting our recommended work practices standard to OSHA made reference to our inability to describe a "safe" exposure level, hence our recommendation was that where any employee is exposed to measurable concentrations of VC as determined by the recommended monitoring method

which has a sensitivity of 1 ppm, he shall be afforded respiratory protection. This does not mean that an "acceptable" level is impossible to define. We have asked the Department of Health, Education, and Welfare Committee to Coordinate Toxicology and Related Programs to define procedures for designing animal studies and to determine the compatibility of the estimated carcinogenic hazard with a socially acceptable risk. These procedures, when developed, should give guidance to experimental design of animal toxicologic studies. In our opinion, the numbers of animals exposed in both the European and American studies have been too small to make statistically valid projections of no effect levels.

The information I will present today is intended to supplement and update NIOSH testimony presented at the February 15, 1974, OSHA Fact-Finding Hearing on Vinyl Chloride. It will cover four areas:

1. Epidemiology and Surveillance
2. Sampling and Analysis
3. Respiratory Protection
4. Exposure Levels

It is hoped that the hearing record can be kept open long enough to enable NIOSH to submit an updated report on current epidemiologic, industrial hygiene, and medical studies. The results of our first industrial hygiene survey will be available in about one month.

1. Epidemiology and Surveillance

On January 22, 1974, the National Institute for Occupational Safety and Health (NIOSH) was informed of three deaths from angiosarcoma of the liver among polyvinyl chloride (PVC) production workers at the B. F. Goodrich plant in Louisville, Kentucky. Since that time, NIOSH has initiated a variety of activities concerned with assessing the extent of the problem and developing information required for effective control of exposure and protection of workers exposed to VC.

Immediately following the report of January 22, NIOSH and its parent agency, the Center for Disease Control (CDC), organized a surveillance network to determine the number and distribution of cases of this rare disease and its relationship to occupational exposure to VC and/or PVC. The detailed results of this activity are shown in attached Table 1. Thus far, 18 cases of angiosarcoma of the liver in PVC production workers and one case in VC monomer production have been confirmed. Thirteen of these cases were reported from the United States and 6 from other countries. All 13 of the U.S. cases and the one from Great Britain have been confirmed histopathologically by the National Institutes of Health. Ten of the U.S. cases are deceased; 3 are living. This distribution of cases from the United States and 4 other countries indicates that we are observing a newly recognized occupational disease associated with exposure to VC, angiosarcoma of the liver. This form of liver cancer has heretofore been quite rare in the general population--only 20 to 30 cases have been reported annually in the U.S. The greater number of occupational cases seen in the U.S. is

probably a reflection of the earlier initiation and greater intensity of surveillance activities here. As regards the distribution in the United States, we have seen that the 13 cases have been reported from a number of plants in different parts of the country. These include 7 cases from the B. F. Goodrich plant at Louisville, Kentucky, 3 cases from the Goodyear plant at Niagara Falls, New York, 2 cases from the Union Carbide plant at South Charleston, West Virginia, and a single case from the Firestone plant at Pottstown, Pennsylvania. Although we are aware of several factors, such as job duties and degree and length of exposure, which may account for differences in occurence, too little information is available at this time to evaluate such differences.

The average age at death for the PVC production workers was 48.5 years which is about 7 years younger than the average age at death from liver cancer in the male population of the United States. The estimated latent period for this disease based on the experience of the 18 PVC production workers is on the order of 20 years. This is consistent with observations on other occupational cancers with latencies varying between 15 and 25 years.

Within the past two weeks, we have also identified two deaths from angiosarcoma of the liver in men employed at plants utilizing PVC to fabricate other products. A summary of the surveillance activities in Connecticut, which led to the discovery of these cases, is given in the CDC Morbidity and Mortality Report for the week ending June 22, 1974.

Although we have accelerated our efforts to identify and evaluate the cases of angiosarcoma of the liver, it will be several months before we can expect to complete this activity.

The evidence accumulated to date on the cancer experience of the polymerization workers, along with the evidence of induction of the same unique tumor in two animal species exposed to VC down to and including 50 ppm, is convincing evidence that these liver tumors resulted from exposure to VC.

During the course of NIOSH/CDC surveillance and epidemiological activities of the past several months, we have become aware of other possible health effects of exposure to VC. Of major importance among these is a disabling liver fibrosis. This condition independent of angiosarcoma has been noted in workers from one of the United States plants and has been observed in almost a third of the men working in one of the German plants. This condition has also been noted in most of the U.S. cases of angiosarcoma of the liver associated with PVC production. It is not yet known whether the fibrosis is a precursor of angiosarcoma of the liver or to what extent it occurs among workers exposed to VC. Clinical descriptions of several of the U.S. cases of angiosarcoma and of hepatic fibrosis are given in the CDC Morbidity and Mortality Report for the week ending February 9, 1974, and in an article by Falk, Creech, Heath, Johnson and Key to be published soon in the Journal of the American Medical Association.

According to an industry sponsored mortality survey of U.S. polymerization workers, this population shows a deficit in overall mortality when compared to the U.S. male population. Yet to be determined is the significance of the report of cancers other than angiosarcoma of the liver which appear to be related to estimated exposure.

As part of its surveillance activities, NIOSH has compiled an extensive bibliography of the world literature on VC (Appendix I) to provide guidance to the Department of Labor, other government agencies and investigators throughout the world who are concerned with this problem.

A NIOSH mortality study is presently underway at 5 PVC production plants, and a medical cross-section survey of current and former polymerization workers and controls is being designed jointly by NIOSH and CDC.

The objectives of the cohort mortality study are 1) to compare the mortality of individuals who have worked in VC plants with that of the general populations; 2) to compare mortality patterns within the population of VC workers, based upon estimated occupational exposure and time since first exposure; and 3) to compare mortality among VC workers with the mortality of other occupational groups. The most time consuming step, vital status ascertainment, is expected to be 85% completed by the end of the summer and totally completed by December on all plants except one.

The major purposes of the medical survey are 1) to determine those diagnostic laboratory procedures best suited for detection of liver disease

among workers at VC polymerization plants; 2) to identify as completely as possible those workers or former workers with liver abnormalities so that they may be referred for appropriate medical evaluation and therapy; and 3) to identify other medical illnesses conceivably related to VC exposure.

2. Sampling and Analysis

The field sampling and analysis method for VC previously recommended by NIOSH with a sensitivity of 1 ppm, required the use of a 250 cc glass gas sampling tube, and subsequent analysis by gas chromatography. Subsequent research by NIOSH has indicated that alternatively a charcoal tube can be used for collection of VC which permits the collection of integrated personal samples. We recognize that gas chromatographic procedures are now available with a sensitivity of several parts per billion, but it should be realized that laboratory instrument conditions are seldom practicable for field use. NIOSH research is continuing in this important area of sampling and analysis.

3. Evaluation of Respiratory Protection

Questions regarding the effectiveness of cartridge and canister type respirators led NIOSH to evaluate the performance of approved respirator organic vapor cartridges and canisters against VC.

Four makes of organic vapor cartridges and 4 makes of organic vapor gas mask canisters were tested against various concentrations of VC at a

flow rate consistent with a moderately heavy work rate. The effect of relative humidity on service life was also investigated.

These tests show a cartridge life, based on 10% break-through, to be 40 to 75 minutes at 50 ppm, 50% relative humidity, depending upon the manufacturer. Also canister life at 100 ppm, 50% relative humidity, was shown to range from 200 to 350 minutes again depending on the manufacturer. It should be noted that the service life decreases as the ambient relative humidity increases.

Gas mask, face piece leakage is typically 1% of the ambient concentration. At 100 ppm ambient concentration, 1 ppm leakage could be expected. Because the odor threshold of VC is considerably higher, a worker would have no indication as to whether he is or is not being adequately protected. Therefore, it is the position of NIOSH that the only suitable respiratory protection devices for VC are supplied air respirators or positive pressure self-contained breathing apparatus.

4. Exposure Levels

The industrial hygiene activities conducted by NIOSH have been directed at determining present and past worker exposure to VC and other liver toxins, and work practices, and control procedures utilized to reduce and eliminate such exposures. These investigations have involved VC production plants, VC polymerization and copolymerization plants and PVC processing (fabricating) plants (i.e., compounding, extrusion molding, calendering, thermoforming,

binding, foams, fibers, and plastisol operations).

Walk-through surveys of one VC plant and 7 PVC plants have been conducted to date. Air sampling surveys for VC have been conducted in 7 PVC fabrication plants and the data herein presented. Also, a detailed industrial hygiene survey of one PVC plant has been conducted but results will not be available until next month.

Polymerization Plants

The walk-through surveys of the polymerization plants were conducted to determine which plants would be selected for the detailed industrial hygiene surveys from which the documentation of worker exposures would be obtained. Process information, plant layouts, air sampling data collected by the plant, work practices and control procedures were noted and obtained during the walk-through surveys. The criteria for selection of the 7 plants were based primarily on the needs of the overall epidemiological study. These criteria required that the plants (1) were in operation for at least 15 years; (2) had a large worker population; (3) were located in States where vital statistics could easily be obtained; and (4) have an "in-house" medical program.

The polymerization plants observed during the walk-through surveys used the suspension, emulsion, and solvent processes. The only process not observed to date is the bulk process. The one plant (from the initially selected 7) where a detailed indutrial hygiene survey has been conducted was selected because of its age (39 years of production), the fact that it is one of only two plants using the solvent process to product PVC, and cases of angiosarcoma of the liver in employees of the plant have been reported.

In the first and second quarter of FY'75, NIOSH will conduct detailed industrial hygiene surveys in at least 3 additional polymerization plants. They will be selected from the 6 remaining plants where walk-through surveys were conducted and from other plants that utilize the bulk process to give a cross-section of the different processes utilized by polymerize VC.

Based on the walk-through surveys of the 7 plants and the one detailed industrial hygiene survey, a brief summary of NIOSH observations is presented in Table 2. This table presents the major sources of VC releases within the PVC plants and work practices and control procedures that can be utilized to reduce and/or eliminate these emissions.

VC (Monomer) Production Plants

The VC plant that was visitied on a walk-through survey used the ethylene oxychlorination process. No plant using the acetylene process has been visited. Due to a limitation of personnel and time, it was decided that further detailed surveys of VC plants would be done under contract. This survey will be completed in June 1975 and will consist of documenting the previously mentioned exposure data, etc. for VC plants based on detailed industrial hygeien surveys of at least 3 plants that will be selected to be representative of the industry.

Based on the walk-through survey of the VC plant, a brief summary of the NIOSH observations about the major sources of VC releases within VC plants and work practices and control procedures that can be utilized to reduce and/or eliminate these emissions is presented in Table 3.

Fabrication Plants

The air sampling surveys of 7 PVC fabrication plants were conducted at the following operations: extrusion, thermoforming, calendering and plastisol processing. In general, any process involving the heating and/or mixing of PVC resin can result in the release of VC.

A compilation of NIOSH's air sampling survey data from 7 PVC fabrication plants is presented in Table 4. Table 5 summarizes the environmental findings from our studies in PVC fabrication plants. Breathing zone samples, that is, actual measured exposures to VC, ranged from 0.3 to 12 ppm with a mean of 3 ppm; and estimated time weighted average (TWA) exposures were approximately 2 ppm. The latter estimate was made by combining "Breathing Zone" samples with "Area" samples.

Peak levels of at least 300 ppm were measured in the PVC fabrication plants. However, extended exposures to such concentrations are quite improbable, since these levels exist only at "contamination sources" rather than at normal work sites. Maintenance and repair workers, however, may be exposed to such levels.

Further data will be available when the aforementioned contract study is completed.

NIOSH's recommended work practices standard was meant originally to be applied to the manufacture of synthetic polymer from VC. In view of the finding of appreciable concentrations of VC in fabrication operations and the reports of angiosarcoma in monomer production and in secondary manufacture, we recommend that exposure to this carcinogen be controlled whenever it is encountered in the workplace.

June 25, 1974

TABLE 1

CONFIRMED CASES OF LIVER ANGIOSARCOMA AMONG WORKERS EXPOSED TO VINYL CHLORIDE OR POLYVINYL CHLORIDE

| COUNTRY | CASE # | BIRTH DATE | 1st VC or PVC EXPOSURE | DX ANGIO-SARCOMA | AGE AT DX | YRS 1st EXP TO DX | TOT YRS EXP | DATE OF DEATH |
|---|---|---|---|---|---|---|---|---|
| **VC MONOMER PRODUCTION WORKERS** | | | | | | | | |
| Sweden | 02 | 11-27-11 | 00-00-45 | 05-15-72 | 61 | 27 | 23 | 08-16-72 |
| **POLYMERIZATION WORKERS** | | | | | | | | |
| United States | 01 | 00-00-22 | 12-09-48 | 03-00-71 | 49 | 22 | 16 | 03-03-73 |
| United States | 02 | 00-00-34 | 11-15-55 | 05-00-70 | 36 | 14 | 13 | 09-28-71 |
| United States | 03 | 00-00-15 | 11-28-45 | 12-00-73 | 58 | 28 | 28 | 12-19-73 |
| United States | 04 | 00-00-24 | 07-06-52 | 08-00-67 | 43 | 15 | 15 | 01-07-68 |
| United States | 05 | 00-00-12 | 06-19-44 | 04-00-64 | 52 | 20 | 18 | 04-09-64 |
| United States | 06 | 00-00-29 | 01-17-62 | 02-00-74 | 45 | 12 | 12 | ALIVE |
| United States | 07 | 05-03-22 | 08-00-44 | 00-00-68 | 45 | 24 | 18 | 03-23-68 |
| United States | 08 | 05-06-20 | 10-07-46 | 08-00-61 | 41 | 15 | 15 | 08-29-61 |
| United States | 09 | 00-00-31 | 05-28-45 | 03-01-74 | 43 | 29 | 17 | ALIVE |
| United States | 10 | 08-16-13 | 06-00-51 | 05-00-68 | 55 | 17 | 17 | 05-10-68 |
| United States | 11 | 05-27-09 | 10-14-46 | 03-00-70 | 61 | 23 | 23 | 03-16-70 |
| United States | 12 | 11-17-18 | 09-13-49 | 05-00-69 | 50 | 20 | 15 | 05-02-69 |
| United States | 13 | 12-01-21 | 08-19-44 | 05-00-74 | 53 | 30 | 30 | ALIVE |
| W. Germany | 01 | 07-26-31 | 10-14-57 | 00-00-71 | 40 | 14 | 14 | 12-14-71 |
| W. Germany | 02 | 06-04-30 | 10-01-57 | 00-00-69 | 39 | 11 | 11 | 01-25-69 |
| Great Britain | 01 | 00-00-01 | 00-00-46 | 12-00-72 | 71 | 26 | 20 | 12-00-72 |
| Norway | 01 | 12-23-15 | 03-00-50 | 12-20-71 | 56 | 22 | 21 | 01-04-72 |
| Sweden | 01 | 06-23-27 | 08-14-51 | 02-00-70 | 43 | 19 | 18 | 10-20-70 |
| **COMPOUNDERS, FABRICATORS, ETC** | | | | | | | | |
| United States | 14 | 00-00-13 | 08-18-38 | 06-00-73 | 60 | 36 | 00 | 07-03-73 |
| United States | 15 | 00-00-25 | 00-00-00 | 07-00-72 | 47 | 00 | 00 | 02-15-73 |

Note: '00' indicates unknown date

Table 2

MAJOR VINYL CHLORIDE EMISSION SOURCES IN POLYVINYL CHLORIDE POLYMERIZATION AND COPOLYMERIZATION PLANTS

| Sources of Vinyl Chloride Emissions | Work Practices and Control Procedures That Can Be Utilized to Reduce And/Or Eliminate the Emissions |
|---|---|
| 1. Polymerization reactor cleaning | a. Reduction in the frequency of cleaning<br>b. Automate cleaning process<br>c. Maximize purging of reactor before and during employee entry into reactor<br>d. Employee use of air supplied respirators (type prescribed by OSHA) when cleaning reactors |
| 2. Venting vinyl chloride from processing equipment internally within the plant | Repipe vented vinyl chloride emissions to a recovery system or completely remove vinyl chloride from vented air prior to release |
| 3. Quality control sampling of process | a. Redesign sampling points to eliminate excess pipe downstream of sampling valves in order to reduce the amount of vinyl chloride lost after sampling<br>b. Employee collecting sample should wear air supplied respirator as prescribed by OSHA |
| 4. Process leaks from such things as pumps, valves, flanges, gaskets, etc. | a. Use direct reading vinyl chloride sampling device on a routine basis for early detection of process leaks<br>b. Change pump seals, agitator packing, etc. to designs better suited to prevent leaks |
| 5. Tank car loading and unloading | a. Eliminate vinyl chloride that is exhausted while loading and unloading tank cars by piping changes and venting to recovery system or completely removing vinyl chloride from vented air prior to release<br>b. Employee use of air supplied respirators (type prescribed by OSHA) while connection and disconnecting lines |

Table 2 (Continued)

| | |
|---|---|
| 6. Vinyl chloride monomer filter changing | a. Reduce frequency of monomer filter changing<br>b. Employee use of air supplied respirator (type prescribed by OSHA) while changing or cleaning filter |
| 7. Polyvinyl chloride waste disposal | Properly cover all polyvinyl chloride waste barrels, drums, bins, etc. |
| 8. Packaging (bagging and drumming of polyvinyl chloride) | a. Improve local exhaust ventilation at bagging and drumming stations to reduce polyvinyl chloride dust and vinyl chloride gas emissions<br>b. Clean baghouses and other control devices frequently to insure top efficiency of ventilation system<br>c. Employee use of air supplied respirators (type prescribed by OSHA) while cleaning baghouse. |

Table 3

MAJOR VINYL CHLORIDE EMISSION SOURCES IN VINYL CHLORIDE MONOMER PRODUCTION PLANTS

| Sources of Vinyl Chloride Emissions | Work Practices and Control Procedures That Can Be Utilized to Reduce And/Or Eliminate the Emissions |
|---|---|
| 1. Tank car loading and unloading | a. Eliminate vinyl chloride that is exhausted while loading and unloading tank cars by piping changes and venting to recovery system or completely removing vinyl chloride from vented air prior to release<br>b. Employee use of air supplied respirators (type prescribed by OSHA) while connecting and disconnecting lines |
| 2. Quality control sampling of process | a. Redesign sampling points to eliminate excess pipe downstream of sampling valves in order to reduce the amount of vinyl chloride lost after sampling<br>b. Employee collecting sample should wear air supplied respirator as prescribed by OSHA |
| 3. Process leaks from such things as pumps, valves, flanges, gaskets, etc. | a. Use direct reading vinyl chloride sampling device on a routine basis for early detection of process leaks<br>b. Change pump seals, agitator packing, etc. to designs better suited to prevent leaks |

Table 4

Exposure Levels of Vinyl Chloride in PVC Fabrication Plants NIOSH Data (summary of 7 Plants) [illegible]

| Fabrication Product | Type Resin | Location and Operations | Conc. PPM | Results Summary |
|---|---|---|---|---|
| . Operators' Breathing Zone Samples (measured exposures) | | | | |
| 1.film | paste | over mixing vessel, dumping bags | 2 | Max. = 12 PPM |
| 2.film | 20 mil film | packing table, behind cutter | 0.3 | Min. = <0.3 |
| 3.film | 12 mil film | packing table, behind cutter | 0.3 | Median =0.3 |
| 4.flex. sheet | suspension | film sealing, operator's position | 12 | Mean = 3 |
| 5.molded products | comped.cubes | molding machine operator | <0.3 | > 1 PPM=2/5=40% |
| . Area Samples (probable exposures) | | | | |
| 1.molded products | comped cubes | trimming table 8 feet from mold machine | <0.3 | Max. = 8 PPM |
| 2. " " | " " | 4 inches from cutter outlet | <0.3 | Min. = <0.3 |
| 3. " " | " " | 12 inches from cutter outlet | <0.3 | Median= 0.3 |
| 4. " " | " " | 24 inches from cutter outlet | <0.3 | Mean = 1.2 |
| 5. " " | " " | 22 inches above hopper | <0.3 | > 1 PPM= 1/11=9% |
| 6.film | 20 mil film | work station near press | 0.5 | |
| 7. " | 12 mil film | side of heater section | 0.3 | |
| 8.molded products | comped cubes | extruder line, next to cutter | 0.4 | |
| 9.film | suspension | mixing area- operation shut down | 0.8 | |
| 10." | suspension | mixing area - operation shut down | < 4 | |
| 11." | suspension | film sealing unit at operator's position | 8 | |
| . Source Samples (possible exposures) | | | | |
| 1. raw material | paste | withdrawing sample from bag | 10 | Max. = 340 PPM |
| 2. " " | suspension | " " " " | 340 | Min. =<0.3 |
| 3. " " | comped cubes | " " " " | <3 | Median = <1 |
| 4. " " | paste | " " " " | 1 | Mean = 18 |
| 5. " " | paste | " " " " | 2 | > 1 PPM=10/21=48% |
| 6. " " | paste | " " " " | <1 | |
| 7. film | paste | withdrawing sample from oven | 1 | |
| 8.film | paste | 6 inches from feed pan on a film coater | <0.3 | |
| 9.molded products | comped cubes | 1 foot above injection molder (4 samples at this spot) | <0.3 | |
| 10." " | " " | 1 inch above injection molder (2 samples at this spot) | 0.3 | |
| 11.film | 20 mil film | near intake to press | 0.5 | |
| 12." | 12 mil film | above inlet to heating section | 0.7 | |
| 13.mold strip | comped cubes | 12 inches from extruder die head | <0.3 | |
| 14." " | " " | feed hopper | <0.3 | |
| [illegible] | " " | [illegible] | | |

Table 5

Summary of Exposure Levels to Vinyl Chloride in PVC Fabrication Plants



| 1. Film and Molded Products (NIOSH Data) | Gas Concentrations-PPM(A) | | | | |
|---|---|---|---|---|---|
| | Max. | Min. | Median | Mean | >1 PPM(B) |
| a. Operator Breathing Zone | 12 | <0.3 | (C) 0.3 | 3 | 2/5=40% |
| b. Area Samples | 8 | <0.3 | 0.3 | 1.2 | 1/11=9% |
| c. Source Samples | 340 | <0.3 | <1 | 18 | 10/21=48% |

(A) PPM = parts of gas per million parts of air mixture
(B) > = greater than
(C) < = less than

Dr. Marcus Key, Director
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Liver - Connecticut
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EPIDEMIOLOGIC NOTES AND REPORTS

## ANGIOSARCOMA OF THE LIVER – Connecticut

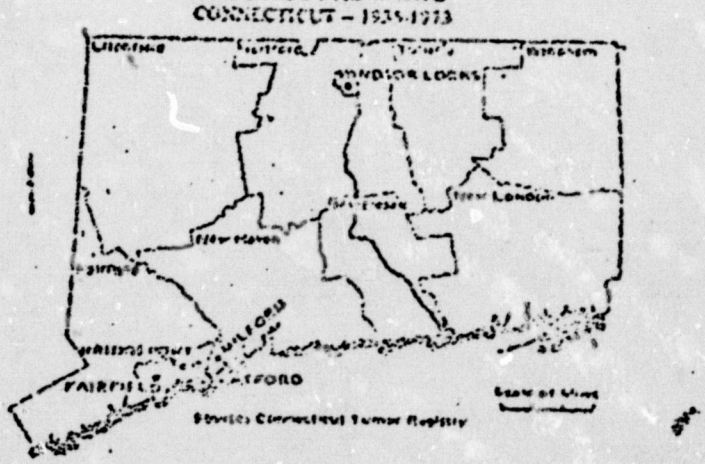
From January 1935 through December 1973, 8 cases of angiosarcoma of the liver were reported to the Connecticut Tumor Registry; the diagnosis of hepatic angiosarcoma has been confirmed in 6 of these cases by pathologists at the National Cancer Institute.

One case was diagnosed in 1950, 1 in 1967, and 4 in 1972 and 1973. The 1950 case occurred in a resident of northcentral Connecticut, while the 5 more recent cases were found in residents of 4 closely adjacent communities in the southwestern portion of the state (Figure 1).

Two of the patients appear to have had occupational exposure to polyvinyl chloride (PVC). One, a 47-year-old man diagnosed in January 1973, had been employed for the 10 preceding years as an accountant in a factory which produces vinyl sheets and processes PVC resins; it is reported that he frequently visited the production area of the plant. Another patient, a 61-year-old man diagnosed in June 1973, had worked from 1933 through 1971 in an electrical products manufacturing concern, and from 1958 through 1963 he had operated

(Continued on back page)

Figure 1
CASES OF ANGIOSARCOMA OF THE LIVER
BY PLACE OF RESIDENCE
CONNECTICUT – 1935-1973



## ANGIOSARCOMA – Continued

machinery there which applied plastics containing PVC to wires as insulating material.

Another 2 patients who had no occupational exposure to PVC had been long-time residents of the Bridgeport-Stratford area. One of these was a 73-year-old man, diagnosed in 1967, who had lived his entire life within 2 miles of the electrical products factory mentioned above. He had worked as a firefighter from 1917 to 1942, as a metal worker from 1942 to 1944, and as a corset cutter from 1945 until his retirement in 1961; additionally he had a history of chronic alcohol ingestion. The other resident was an 83-year-old woman, a housewife and retired cook, who was diagnosed in December 1973. She had lived for 35 years within 1/2 mile of the vinyl products plant.

There was no history of occupational or of potential community exposure to PVC for the 2 remaining patients. One was a housewife in north-central Connecticut, the other an unemployed, disabled man with chronic alcoholism who had moved to Connecticut from New York City 4 months before his diagnosis in May 1973. None of the 6 confirmed patients had known exposure to thorium dioxide (*1*) or to arsenical compounds (*2*), 2 materials known specifically to induce angiosarcoma of the liver in man. By history, none had excessive exposure to aerosol sprays. None had a past history of hepatitis. Two had histories of alcoholism, as noted, but none are known to have taken other potentially hepatotoxic drugs or medications.

*(Reported by Sorkeen W. Christine, M.D., Chief, Chronic Disease Control Section, Harold S. Barrett, M.D., Deputy Commissioner of Health, and Douglas S. Lloyd, M.D., Commissioner of Health, Connecticut State Department of Health; the National Institute of Occupational Safety and Health, and the Cancer and Birth Defects Division, Bureau of Epidemiology, CDC.)*

**Editorial Note**

Recent reports (*3,4*) have described 13 cases of angiosarcoma of the liver among men engaged in the synthesis of PVC from vinyl chloride monomer (VCM). There is evidence to suggest that VCM may have been the cause of these angiosarcomas in these cases (*5,6*). In the present report, cases of hepatic angiosarcoma are described in men who had no known exposure to VCM, but who did work with PVC. While these findings establish no causal connection between exposure to PVC and angiosarcoma of the liver, they do raise the possibility of such a relationship. Further studies throughout the nation will be needed to define the possible risk factors in persons who have worked with PVC.

The additional finding in this study of angiosarcoma of the liver in 2 persons who had no occupational exposure to vinyl chloride, but who may have had community exposure, is also worrisome but again establishes no causal connection. It might be expected on the basis of data from the Third National Cancer Survey that approximately 4 cases of angiosarcoma of the liver would occur in Connecticut in a 10-year period and that approximately two cases would occur in the 4 previously mentioned communities in southern Connecticut during the same interval. Epidemiologic investigation of additional cases of hepatic angiosarcoma that may be found to have had possible community exposure to vinyl chloride will be necessary to clarify the significance of these cases.


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The data in this report are provisional, based on weekly information to CDC by state health departments. The reporting week ended with receipt of reports of cases or deaths received by 4:30 p.m. (EST) on the date indicated at the head of the table of contents.

Address all correspondence to: Center for Disease Control, Attn: Editor, MMWR and Morbidity and Mortality Weekly Report, Atlanta, Georgia 30333

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# A BIBLIOGRAPHY ON VINYL CHLORIDE

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Arch Env Health - Archives of Environmental Health
Arch Tox - Archives of Toxicology
Arkh Path - Arkhis Patologii (Archives of Pathology)
Arch Derm - Archives of Dermatology
Arch I H and Occ Med - Archives of Industrial Hygiene and Occupational Medicine
AIHAJ - American Industrial Hygiene Association Journal
Biochem J - Biochemical Journal (England)
Br Med J Bul - British Medical Journal Bulletin
Br J Derm - British Journal of Dermatology
Br J Ind Med - British Journal of Industrial Medicine
Bull of Hyg - Bulletin of Hygiene
C.A. - Chemical Abstracts
Can Med Assoc J - Canadian Medical Association Journal
Chem Eng - Chemical Engineering
Clin Chem - Clinical Chemistry
Env Res - Environmental Research
Farmakol Toksikol - Farmokalogiia i Toksikalogiia (Moscow)
Gaz Woda - Gaz, Woda i Technika Sanitarna (Polish)
Gig Sanit - Gig i Sanit (USSR)
Gig Truda - Gigiena Truda i Professionlnye Zabolevaniya (USSR)
Hyg and Sanit - Hygiene and Sanitation (USSR)
J Chem Eng Data - Journal of Chemical and Engineering Data
J Occ Med - Journal of Occupational Medicine
J Pharm Sci - Journal of Pharmaceutical Sciences
J NCI - Journal of the National Cancer Institute
J App Chem - Journal of Applied Chemistry
JAMA - Journal of the American Medical Association
JMA Georgia - Journal of the Medical Association of Georgia
Lancet - The Lancet (British)
Labor Hyg and Occ Dis - Labor Hygiene and Occupational Diseases (USSR)
Med Lav - Medico Lavoro (Milan)
NE J Med - New England Journal of Medicine
T & AP - Toxicology and Applied Pharmacology
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middle of the afternoon, which he must catch. I would appreciate having the questions for Dr. Lloyd first, if that is agreeable with you, Your Honor?

JUDGE MYATT: Fine.

Is he going to make a presentation?

MR. KEY: No. Mine will be the only presentation.

JUDGE MYATT: All right. Then the copy of the presentation, Madam Reporter, will be Exhibit No. 13.

(Exhibit No. 13 was marked for identification and received in evidence.)

JUDGE MYATT: Do you have any questions from the Department of Labor?

MR. KLEIN: Yes, I do, your Honor -- a few brief ones.

In the course of Dr. Key's presentation, mention was made to an industry-sponsored study at the Epidemiological Survey.

Am I correct in assuming that is the Tabershaw-Cooper Survey?

DR. KEY: That is correct.

MR. KLEIN: Mr. Lloyd, I take it that this is your area. I will ask you this question.

Would you give us a brief analysis of that study, please?

DR. LLOYD: There are a number of limitations in this study which I might point out, Drs. Tabershaw and Gaffey do point out. I don't think they emphasize some of these deficiencies as strongly as I would. The index-of-health response that they use is the ratio of the number of observed deaths to the number of expected deaths from each of the causes.

They point out that, over-all mortality is only 75 percent of expectation, and they do note, for a number of cancer sites, there is an excess, but they say it is not statistically significant.

The greatest limitation in this study is that some of the deficiencies in it tend to increase the number of expected deaths, and to decrease the number of observed deaths so that all of these standard mortality ratios, I would assume are underestimated.

I don't think we can talk about the statistical significance of these deficits.

As an example, they point out that 15 percent of the total population under study was not traced; that the population that was not traced was, in general, eleven years older and had eleven years longer since exposure.

The median exposure for those that were not traced, according to their exposure index, was higher for those that were not traced than for those that were; and they note that a large group of 1500 workers with 35 years since exposure, were

not included in this study.

Finally, the study of men who worked both in synthesis of vinyl chloride, and in polymerization, and we don't know what the mix is. From the data we have at hand at this point, it would appear that polymerization workers are showing a greater rate of this disease, so the weighing of VC and PVC workers might have an effect.

In the case of the over-estimation of the expected deaths, the general population mortality is used to estimate the expected deaths. We recognize generally in occupational health that we would see, in comparing an industrial population to a general population, that we will see deficits, because men are selected out for health, because they are employable.

Furthermore, in this study, since men were included in the study who had at least one year of exposure up to December 31, 1972, we would have had a continued influx into the population of people who had to be selected for employability and therefore would be healthier.

Drs. Tabershaw and Gaffey do point out that they saw excesses at higher exposure levels for cancers of the respiratory system, the brain, lymphosarcoma, and the digestive system, which was primarily cancer of the liver -- seven liver cancers.

I would say that the information that they have provided is certainly not information that can reassure us on the question of carcinogenicity of vincyl chloride, and I think

m/rew there is a distinct possibility, from looking at their data, that we may see malignancies other than angiosarcoma of the liver in this population.

110 MR. KLEIN: Your Honor, in light of Dr. Key's request with respect to Mr. Lloyd, I would prefer not to ask further questions at this time, and allow Mr. Lloyd to answer any questions from the audience, and then he could leave.

JUDGE HYATT: All right. Yes, sir?

MR. TOPOL: If I may, please.

With regard to the cases of angiosarcoma in the United States, those cases have been reported among employees in 13 different plants; is that correct?

DR. LLOYD: No, at four different plants, to date.

MR. TOPOL: Four. It's 13 employees at four different plants in the United States?

DR. LLOYD: At four polymerization plants. And two cases to date from plants engaged in fabrication.

MR. TOPOL: Concentrating on the ones that have been developed at the PVC plants, how many plants are there in the United States that are 20 years and older?

DR. LLOYD: I don't think I could give you that number. I know there are 37 plants in total. I think the plants that we have seen this from so far as the plants that have been on line the longest. But even in the case of these plants, we have yet to track down the total population. So I don't know what we can

say at this point.

MR. TOPOL: Well, would you accept my view that there are eight plants that fall into that class? Is that approximately right?

DR. LLOYD: I would accept that.

MR. TOPOL: If the employee exposure to vinyl chloride is what caused the angiosarcoma, then wouldn't you expect the number of cases to be reasonably randomly divided over the plants that fit into that class of 20 years and older?

DR. LLOYD: Well, you have to remember, first of all, that you are looking at an extremely rare tumor. Where most of the cases did not become evident until 1968. Of the 21 angiosarcoma that have been seen to date in the United States and the four other countries, 13 of these were diagnosed in 1968 or later. So this thing is just beginning to break out. I don't think we have enough information to talk about a random distribution.

MR. TOPOL: No, but what I'm asking is, you would expect a random distribution, wouldn't you, assuming the angiosarcoma was the cause of the --

DR. LLOYD: Depending on what the exposure level was at those plants.

MR. TOPOL: Okay. But if you had a reasonably even exposure limit, then you would expect a random distribution among the plants in terms of the cases of angiosarcoma.

DR. LLOYD: All right.

MR. TOPOL: Well, if you didn't, if you end up with this distribution that shows a very large number at one plant, and none at many others, in the class 20 years and older, what conclusion do you offer as to why this might occur?

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DR. LLOYD: I don't think we can say that we're looking at a non-random distribution. There are many other cases yet to be identified. We have just begun to scratch the surface on this.

MR. TOPOL: Well, you are talking, though, and I think it was the direct testimony, there were seven at one plant.

DR. LLOYD: Seven from the Louisville plant.

MR. TOPOL: That's right.

DR. LLOYD: The Louisville plant is where this was first identified by Dr. Creech, and there has been a much more intense investigation there. But even in Louisville we haven't tracked down yet the men who left employment there, to see what has happened to them.

MR. TOPOL: Okay. But my question to you is: If you don't have a random distribution, then what is the explanation for that?

DR. LLOYD: There could be a great variety of explanations. It could have to do with the job assignments, it could do with variations in exposure, length of exposure, many things.

MR. TOPOL: What do you mean when you say the "variation of exposure"? You mean that some employees were subjected to

higher levels than others?

DR. LLOYD: Yes. Yes.

MR. TOPOL: And that employees subjected to a lower level were not subjected to a sufficiently high level to contract angiosarcoma?

DR. LLOYD: No. They'd contract it, but later in time. A longer latent period.

MR. TOPOL: But at least that the difference of exposure becomes a perhaps critical variable, if we have the lack of random distribution?

DR. LLOYD: The degree of response would be a function of the amount of exposure.

MR. TOPOL: You also testified -- I guess I should direct this to Dr. Key, if I could.

JUDGE HYATT: Well, you cannot. We're only going to question Dr. Lloyd.

MR. TOPOL: Okay. Thank you.

JUDGE HYATT: Any other questions?

MR. HECKMAN: Doctor, I notice that in the table dealing with angiosarcoma deaths among workers under compounder -- you have two deaths listed under compounders and fabricators.

DR. LLOYD: That's right.

MR. HECKMAN: And apparently the table is tending to indicate that these are confirmed cases of liver angiosarcoma, and a relationship is established between them and exposure to

vinyl chloride or polyvinyl chloride.

DR. LLOYD: I don't think you're quoting us correctly on that. I think Dr. Key pointed out that the information on the two cases is insufficient to say what the extent of the problem could be among the fabricators. We do point out that having seen the persons exposed to vinyl chloride are showing a very high rate of this disease, we now have begun to identify people who might have had considerably lower exposures than this initial population.

Both of these cases were confirmed at the National Institutes of Health, as angiosarcoma of the liver. Both of these men worked in environments where there would have been exposure to vinyl chloride.

What we say at this point, we are not willing to say how serious the problem could be in fabrication; we want more evidence.

MR. HECKMAN: In other words, you're not denying this part about morbidity and mortality weekly report, also submitted with Dr. Key's testimony, to the effect that no causal connection has been established between those workers in the fabricating plants and the PVC?

DR. LLOYD: I don't think we say anything about causal connection. I think we did say that the evidence at hand shows that vinyl chloride induces angiosarcoma of the liver.

Here is a population that had low exposure to vinyl

chloride, and here is the evidence to date on the health effect. We do not know what the extent of the problem is yet in fabrication.

MR. HECKMAN: Well, in this report that's attached to Dr. Key's statement, it's indicated that, with regard to these two other cases, the findings establish no causal connection between exposure to PVC and angiosarcoma of the liver.

I can assume that that is a part of the testimony, and that the inclusion of these two cases in the table is not intended to indicate a causal connection, despite that statement. Is that correct?

DR. LLOYD: If I can try to interpret for you what they are saying in that report.

MR. HECKMAN: I'd appreciate it.

DR. LLOYD: They're saying in this specific case, in the single individual case, if a person dies of angiosarcoma of the liver, he could have been exposed to many things. He could have been exposed to thorotrast, to arsenic, to other things that might have caused this disease. We have recent evidence that indicates that vinyl chloride produces these tumors in great number. And part of the development --

MR. HECKMAN: In great number?

DR. LLOYD: In great number, very great number for this population.

When you're looking at a disease where you would only

see 20 or 25 deaths from this disease in a year in the population in the United States, and we have now have identified in the United States alone 15 cases associated with this kind of exposure, I think this is a very, very serious problem. This is a great response.

MR. BECKMAN: Do you believe that that could in any degree be possible, to the fact that looking for angiosarcoma in the past, in the general population as well as among PVC workers, may have been a bit less intense?

DR. LLOYD: We have no evidence that any recent looking for cases would have brought this out.

MR. BECKMAN: Well, I'm not certain -- if this is not to be directed to you, I assume you will tell me, and I will sit down and wait to direct it to another witness.

But are you in a position to inform us as to whether or not it's common practice for the medical profession to examine patients who have died of liver disease on an in-depth basis to determine whether or not the disease may have been angiosarcoma?

DR. LLOYD: I don't know how germane that might be, but we do know that, for a number of these deaths, there has been mis-diagnosis and mis-reporting of cases.

MR. BECKMAN: And that could be true for the general population as well?

DR. LLOYD: Oh, yes. Yes.

MR. HECKMAN: In other words, it's quite possible that many deaths from liver disease, which are diagnosed as cirrhosis necrosis, general hepatoma, or any similar liver ailment, could conceivably involve angiosarcoma, if the investigation were intense enough?

DR. LLOYD: I can only say my impression from the people I have talked to is that that wouldn't be a great number. Perhaps instead of 25 you might have 50.

MR. HECKMAN: But that is a possibility?

DR. LLOYD: Oh, yes. Sure.

MR. HECKMAN: Are you familiar with the techniques necessary to determine whether you have got angiosarcoma or not?

DR. LLOYD: No, you'd have to talk to a pathologist on that.

MR. HECKMAN: Okay, then that eliminates your part of the questioning. Thank you very much.

[Announcement.]

JUDGE HYATT: Yes, ma'am.

MS. HRICO: Andrea Hrico from the Health Research Group.

Dr. Lloyd, you mentioned the industry-sponsored mortality study done by Tabershaw and Gaffey. Do you know if that study was strictly limited to plants where workers were first exposed to vinyl chloride more than 20 years ago?

DR. LLOYD: No, they don't identify the plants. They

per million, plus or minus 50 percent in the field?

DR. HARRIS: Yes. There are such -- I'm Elliott Harris, Director of the Division of Laboratories and Criteria Development, NIOSH, Cincinnati.

Yes, there are such methods, methods are based primarily upon gas chromatographic analysis, that's separation and analysis. The analytical procedures themselves have precision of roughly 5 percent -- that is reproducibility; and they have an accuracy of approximately the same 5 percent. That is, within 5 percent of the actual concentration.

MR. KLEIN: I have no further questions at this time, Your Honor.

JUDGE MYATT: Yes, sir?

MR. CONNOLLY: Dr. Key, is there any evidence as to the effect on humans of exposure to concentrations of VCM under 50 parts per million?

DR. KEY: Evidence of exposure to humans, of exposure --

MR. CONNOLLY: As to the effects on humans, of the concentrations --

DR. KEY: As to the effect on humans of exposure of vinyl chloride under 50 parts per million.

There are some studies, I believe in the Russian literature, of some effects. These are --

MR. CONNOLLY: I'm referring to studies that result in cancer.

DR. KEY: Headaches and neurotic disturbances have been described at relatively low concentrations. But other than this, I can't tell you of any.

MR. CONNOLLY: Is there any evidence, at 50 parts per million, of any effect on animals, by any studies that you've come across or anybody you know has come across, that have led to a conclusion that cancer can be caused at levels below 50 parts per million?

DR. KEY: No. The closest thing would be the extrapolation that you heard Dr. Schneiderman give this morning from effects observed at 50 and higher parts per million.

MR. CONNOLLY: I think you indicated in your speech that there were not a significant number of mice or rates to draw a proper analysis. Is that correct?

DR. KEY: Well, that wouldn't invalidate what Dr. Schneiderman is saying. It would -- I said that to point out that a no-effect level would be questionable, because of the small number of animals in that exposure cell.

MR. CONNOLLY: It is scientifically accepted, is it not, that the basis on which to extrapolate the carcinogenic effects on rats and mice of a chemical substance to human experience is qualitative and not quantitative. Isn't that correct?

DR. KEY: Well, there's all kinds of disagreement as to how it would extrapolate. You heard Dr. Schneiderman talk

about three different methods. There are others in addition to these, that he briefly mentioned.

MR. CONNOLLY: If you analyzed the --

DR. KEY: Any method is hazardous.

123 MR. CONNOLLY: If you analyzed the Maltoni studies and the Bio-Test studies, can you draw a conclusion that at least the results created in Bio-Test and the results resulted in Maltoni are not the same for rats and mice, and therefore there is a dichotomy between various species?

DR. KEY: Well, I'd agree that there is a dichotomy among species; but I think it's remarkable that the two have agreed, I mean, have both produced these tumors at 50 parts per million. It's --

MR. CONNOLLY: What about at the higher levels?

DR. KEY: There is no doubt about it, there is a difference in the species' response at different levels. The unusual thing is that you get approximately the same response down at 50.

MR. CONNOLLY: Is it not possible that at very low levels the concentration, the latency period might be extended beyond the life expectancy of humans?

DR. KEY: Yes, indeed. And this is the basis on which an acceptable level is sometimes justified, that the individual or the animal won't live long enough to have overt cancer develop.

MR. CONNOLLY: Are you suggesting, then, that perhaps

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additional studies ought to be made, until a definite level can be arrived at?

124 9 DR. KEY: Well, I'd hate to postpone controls until we had everything demonstrated and experimented toxicology to everyone's approval. I think eventually we will be able to come up with generally agreed-on procedures for estimating the number of animals to be used, and the concentrations; and from this we can figure the reliability.

But it may be academic in the vinyl chloride situation. We are getting down pretty close to zero in the animal effects, and by the time you do establish a valid no-effect level, with a large number of animals, and crank in a safety factor, you're going to be pretty close to zero.

MR. CONNOLLY: Let me ask this question. For all practical purposes, from a medical standpoint, is there any difference in the effects and the exposure levels, say, 15 parts per million and an exposure level of, say, 20 or 25 parts per million? Or would you generally expect that the same results would occur at either 15 or 25?

DR. KEY: I have no basis on which to answer that, other than the slope of the theoretical curve that applies to laboratory animals. Yes, that was mentioned this morning.

MR. CONNOLLY: Has your organization done any studying as to whether or not there is, in fact, any distinction between, say, 10 and 15 or 15 and 20 parts per million?

DR. KEY: No.

MR. CONNOLLY: I see. Just a few more questions.

Has your organization done any engineering or technological studies to determine the feasibility of making the changes that you outlined at Table 2 of your presentation?

DR. KEY: Yes and no. We have observed a number of procedures that minimize or prevent exposure to vinyl chloride, and these are presented in that and other tables. But if you're asking have we followed through and done a formal, technical and economic feasibility study, the answer is no.

MR. CONNOLLY: I see. Okay, thank you very much.

JUDGE MYATT: Yes, sir?

MR. HECKMAN: Dr. Key, if I can direct your attention to Table 4 -- it might be necessary for somebody -- I'm not sure who did this work, so anybody who can help, it would be helpful.

That table deals with Exposure Levels of Vinyl Chloride in PVC Fabrication Plants. I'm wondering if you could tell us -- the table is strange, for a couple of reasons. There seems to be one result in every group that sort of throws the thing off. Most of the other results are virtually non-detectable or something that would be below even the proposed permanent standard.

I wonder if anybody could tell us whether, directing your attention to A-4, for example, under Flexible Sheet, Film

MR. JONES: I would say that over-all this would probably be a typical figure, but there are much higher ones.

MR. HECKMAN: Okay. Thank you.

Were duplicate samples taken at the same time and place, or are these just one-time samples?

MR. JONES: Both. Some of them were duplicates, some of them not.

MR. HECKMAN: But was this 12 figure a duplicate? Duplicated?

MR. JONES: It was -- we took a duplicate sample by another means, and the sample was, there was a problem analyzing it.

MR. HECKMAN: There was some what?

MR. JONES: There was some problem analyzing it.

[MR. HECKMAN:] I see. Okay. I won't press you on that.

I do want to point out that we are concerned about the fact that the table listing the deaths includes those two fabrication plants, when the evidence we've heard so far indicates that the people hardly worked anywhere near VCM, and that the measurements for fabrication plants seemed to be extremely low, and we hope you're not drawing conclusions that aren't warranted there.

I would like to direct these questions, which I attempted to ask before, to some extent, to whoever on the panel is more medically qualified.

A good bit of this case depends on the assumption that angiosarcoma of the liver is a rare disease, and I don't doubt that it probably is. What we aren't certain of is the degree to which there is a search for angiosarcoma in the general population.

Can any further light be cast on that by any part of the panel?

Maybe the best way for me to ask the question is whether I can -- if I can inquire as to how you go about determining whether there is angiosarcoma of the liver. What's the procedure?

DR. KEY: It is a space-occupying lesion in the liver. It's more frequently diagnosed after death than before. During life, a biopsy is required. After death, it's typical for the pathologist to make multiple cuts through the liver, looking for any kind of space-occupying lesion.

I don't think the problem is so much finding a space-occupying lesion, pathologists do a pretty good job of this. The problem you may be alluding to is diagnosing it after they get it out.

You are correct in that awareness of pathologists regarding this rare liver tumor has been increasing over the years. You go back, I think, fifty years ago and it wasn't reported, or it was reported under many different names. And it is a difficult tumor to diagnose. That is why we've had all

of the U. S. cases confirmed by the two top experts in the country.

MR. HECKMAN: These were the vinyl chloride cases?

DR. KEY: Yes, but as Dr. Lloyd pointed out, even though you admit a several-orders-of-magnitude mistake, or under-reporting of angiosarcoma of the liver in the general population, a clustering of this degree in a work population is extremely suggestive that there is an occupational relationship here.

MR. HECKMAN: Well, we're certainly not suggesting that it be ignored, it's just that it begins to irritate after a while to keep hearing this referred to as an extremely rare liver disease, when we think perhaps maybe a contribution has been made to the profession by pointing the doctors at the idea of looking for angiosarcoma in general now. And that might be somewhat helpful.

In any event, I think the point is made.

The only other question I guess I did have, Doctor, I'm not sure this isn't a duplication, is: Is it frequent for doctors to differ in their diagnosis of this type of case?

DR. KEY: Quite.

MR. HECKMAN: In other words, one doctor is apt to call something angiosarcoma, and another to disagree?

DR. KEY: Yes.

MR. HECKMAN: Thank you.

JUDGE MYATT: Yes, sir?

MR. SAMUELS: My name is Sheldon Samuels, Industrial Union Department.

I have a question for Dr. Key. In your statement you refer to your memorandum of March 11, 1974, in which you make reference to your inability to describe a safe exposure level.

Is this inability unique to this carcinogen? And is this unique to occupational health?

DR. KEY: I guess the answer depends on your definition of "safe".

According to the one-hit theory of oncogenesis, no level is safe. The government facility at Pine Bluff, Arkansas is conducting experiments to produce information in the slope of the curve near zero. And only after the results of these -- and it will take many years -- are available, can we come anywhere near answering your question.

That's why I used another term in my testimony, and that is an "acceptable" level, which gets away from the safeness concept.

No, I don't know what a "safe" level is for vinyl chloride, and I suppose this would apply for other carcinogens as well.

MR. SAMUELS: The second part of the question was whether this principle, which you've described, is unique to occupational health. Isn't it true that in other areas of public health, food and drugs, et cetera, we have the same problem, and

that any inability to see this as a single problem is to call for a double standard?

DR. KEY: The principle should be the same, no matter whether it's food, air, whatever.

JUDGE MYATT: Are there any other questions of the NIOSH panel?

Yes, sir.

MR. FLEMING: My name is Fleming, with Air Products and Chemicals.

Dr. [illegible], in your walk-through examinations of the industrial facilities you've seen, was it your impression that a non-detectable level of vinyl chloride could be achieved in those facilities?

DR. KEY: No, we certainly did not get that impression. You perhaps mistake the thrust of our recommendation.

MR. FLEMING: No, I think I understand that. I am asking for a different point of view here, and I think you've already expressed it. That's sufficient for my purposes, at least.

I would like to return again to this matter of statistics of angiosarcoma in the general population.

Do you feel that the examination of the cause of death on death certificates, for example, is an accurate way of determining the incidence of angiosarcoma in the general population?

DR. KEY: It's the best we have. There are many, many difficulties with it.

MR. FLEMING: Would you think it was accurate, or probably understating the real situation?

DR. KEY: I think it understates the real situation in every disease.

MR. FLEMING: Can you say how many of the known cases of angiosarcoma in the PVC situation were found only on retrospective study that went beyond the death certificate statement?

DR. KEY: Many of them were. I can't give you the exact number.

MR. FLEMING: A fairly high percentage, would you say?

DR. KEY: I think in the Tabershaw-Cooper study there were two found by death certificates, and four or five more in addition to that.

MR. FLEMING: So that your comment earlier that several orders of magnitude, one order of magnitude is 10, two is 100, and so on, times what is currently believed to be the general incidence in the public might in fact more nearly represent the case. That's a possibility, at least, I gather you said?

DR. KEY: I wouldn't want to comment on that.

MR. FLEMING: Okay. With regard to these fabricator cases again, I think they are extremely important if --

DR. KEY: You said "fabricated" cases?

[Laughter.]

MR. FLEMING: Well, I hope you haven't gone that far!

But in the cases where we are talking about people exposed in fabrication facilities, these are very important cases, and I gather what you've said is that they are confirmed cases of angio, there's little doubt about that. Is there anything at all in the examination procedure of these cases that would indicate something peculiar to an angio related to vinyl chloride exposure?

Can one differentiate between an angio due to vinyl chloride and any other reason?

DR. KEY: There is one thing, and that is the -- frequently there is a fibrotic condition, which is also seen in the liver along with the angiosarcoma.

Now, this doesn't happen in every case, apparently; but when the two occur together, I think it reinforces our feeling that vinyl chloride was responsible.

133 MR. FLEMING: Can you offer any testimony about whether this was true of either of those cases or not?

DR. KEY: No, I can't, but I can find out and enter that into the record.

MR. FLEMING: I think that would be a useful addition, and I'd appreciate it, sir. Thank you.

JUDGE HYATT: Yes, sir?

MR. TOPOL: My name is Allen Topol, representing Tenneco Chemicals.

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Directing your attention, if I can, Dr. Key, to Table 2 attached to your statement. And first to the text on page 10, which accompanies that statement. Is it correct -- am I correctly reading or understanding your statement to mean that Table 2 was compiled based upon -- what? It says a walk-through survey of seven plants. Is that the basis for the compilation of Table 2?

MR. JONES: Primarily.

MR. TOPOL: Okay. Let me ask you then, when you say -- what do you mean when you say a walk-through of the plants?

MR. JONES: Well, in this case, the walk-through survey involved two industrial hygienists spending two days at each of these plants, both actually going through the facilities collecting information about the processes, changes that occurred, and that sort of thing.

MR. TOPOL: Did you do that yourself, sir?

MR. JONES: Much of it, yes.

MR. TOPOL: And what is it that you observed that led you to arrive at this Table 2? You said there was some other information, that the walk-throughs were the primary source of information. Was there any other source of information?

MR. JONES: Well, I would say that the walk-throughs, plus just personal contact with other industrial people.

MR. TOPOL: Did you have any discussions with equipment

manufacturers as to the possible availability of equipment?

MR. JONES: No, sir.

MR. TOPOL: And did you have discussions with technical personnel at the plants that you walked through?

MR. JONES: Yes.

MR. TOPOL: And did those individuals inform you that -- what, that these steps could feasibly be taken?

MR. JONES: In many cases these steps were already being taken by some of these plants, and in other cases we were informed that these were steps that would be taken by the plant, or that could be.

MR. TOPOL: What, then, does this Table 2 represent? Does it represent the steps that, in the judgment of NIOSH, could feasibly be taken by industry to reduce exposures? Is that what it represents?

MR. JONES: Yes.

135 MR. TOPOL: And did you reach any judgment, or have any judgment made by the employees with whom you talked, as to what the ambient level of exposure in plants would be after these steps were taken?

MR. JONES: No.

MR. TOPOL: Let me ask you one other question in connection with the Table. There's a reference to processing leaks from pumps and so forth. I assume you're talking about high-volume pumps in this connection?

MR. JONES: What are you referring to as high-volume pumps? It's the normal process pumps that they're using to pump both vinyl chloride or, in some cases, the slurry of the product from one place, one tank to another.

MR. TOPOL: Okay. Well, is your judgment that there are pumps, valves, flanges, gaskets available that are leak-free, at the levels of volume that are being carried in a PVC plant?

MR. JONES: In discussions with technical people at some of these plants, they seem to feel that there were such pieces of equipment that were better suited to the task than the equipment that was currently being used.

I don't know that it could be stated that these would be completely leak-free all the time.

MR. TOPOL: Well, wouldn't it be fair to say that there aren't now in commercial availability pumps, valves and flanges that are leak-free at the volume we're talking about?

MR. JONES: I would think so.

MR. TOPOL: What about the loading and unloading of the tank car? Is it possible, from your walk-through in these plants, to perform that loading and unloading operation without some exposure to vinyl chloride monomer being unavoidable?

MR. JONES: I would say in most cases there would be some exposure to a small amount. This is one reason for the recommended use of air-supplied respirator while the employee is

actually connecting or disconnecting his tank car, while he is actually right on top of the tank car.

MR. TOPOL: But that assumes, doesn't it, that that exposure is limited to those employees who are doing the unloading, and since we can't limit the movement of air, isn't it possible that that amount, which you admit will leak out, will inevitably move in other places in the plant site?

MR. JONES: Well, this is one reason for some of the other changes, such as the piping changes, to prevent venting to the atmosphere. I think that these levels can be reduced to extremely low levels.

137 MR. TOPOL: Do you have any judgment as to what, in your opinion -- now, you said that some of the steps on your Table 2 had already been taken by the manufacturing plants. Is that correct?

MR. JONES: Yes.

MR. TOPOL: So that they had already reduced exposures.

Do you have any idea as to what the level of exposure would be, if all the steps in your Table 2 were taken?

MR. JONES: No.

MR. TOPOL: Thank you, sir.

JUDGE HYATT: Are there any more questions of the NIOSH panel?

MR. KLEIN: Your Honor, I have one very short question.

Dr. Key, you mentioned that doctors may disagree on

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diagnosis of angiosarcoma of the liver. Would pathologists disagree among themselves concerning a tumor presented to them which was an angiosarcoma?

DR. KEY: Yes. Even this is possible among pathologists. And this is why we have gone to the two best liver pathologists in the country to confirm the U. S. cases.

MR. KLEIN: Thank you.

JUDGE MYATT: All right. There doesn't seem to be any more questions.

Thank you, Dr. Key, and all of those who accompanied you.

We will take a brief recess, and when we resume the panel will consist of the United Rubber Workers.

[Brief recess.]

JUDGE MYATT: Let's proceed, please.

The next presentation is going to be given by the United Rubber, Cork, Linoleum and Plastic Workers of America.

The gentlemen will be introduced by Mr. Sheldon Samuels of the Industrial Union Department. Mr. Samuels.

STATEMENTS OF [illegible], PRESIDENT, UNITED RUBBER WORKERS AND CHAIRMAN, AND [illegible], DIRECTOR OF HEALTH AND SAFETY; AND LOUIS S. ORLESKY, UNITED RUBBER WORKERS, DIRECTOR OF INDUSTRIAL UNION; ACCOMPANIED BY SHELDON W. SAMUELS, AND, DIRECTOR OF HEALTH, SAFETY AND WELFARE DEPT.

[MR. GOLDBERG: Yes, Mr. Myatt. President Bommarito's statement represents the position of the Industrial Union Department, and because of the fact that he is also a vice-president of the AFL-CIO and because of the wish of the Executive Committee of the AFL-CIO, Mr. Bommarito's statement represents their wishes in this matter. Mr. Bommarito's statement effectively represents the position of the entire AFL-CIO.

MR. BOMMARITO:] Before beginning my formal statement, I would like to make an observation. We are dealing with the question of death and disease, with decisions which will determine the very direction in which our technology will develop. Few Administration hearings are as important as this one. We are asking our government to make decisions that would test the wisdom of a saint. The behavior of the plastics industry is inappropriate. They have established a vinyl chloride information center in the Washington, D.C. They have enriched salesmen on the press

[Ventilation approaches to the control of this compound are standard and while they are not subject to the precise prediction of results, sufficient design options exist to ensure control for materials deemed highly toxic. In the past, the problem has been that of characterizing this compound as a low toxicity one and adopting control measures consistent with this designation."

In plain language, this eminent engineer is saying that industry can not effectively design ventilation systems for more than zero anyway!

In the few operations where this kind of engineering control may not be applicable, personal protective equipment can be used, if the equipment is designed and used properly.

I can not say that some of the older marginal monomer and polymer plants will not have difficulties justifying major alterations. But if management wants to continue to use these plants, the changes will have to be accomplished as quickly as physically possible. Newer plants have a different problem, characterized by the will, not the ability, to do the job.]

Our information is that there are only a few isolated problems in secondary and tertiary production. These problems can be solved.

"Detectable level" is defined in the proposal as

testimony, the first full paragraph, where Dr. Nicholson has suggested that "17 percent of the deaths that have occurred are causally related to exposure to vinyl chloride..."

Do you know what the basis of that statement is?

MR. BOMBARITO: Yes. He is here and will be testifying next and could answer this directly--but this was in his paper, it is a direct quote--in his paper at the meeting in New York City sponsored by the Academy of Sciences and the Society.

MR. KLEIN: Well, since Dr. Nicholson will be here, I will direct that question to him.

Now, have you taken any epidemiological studies with respect to vinyl chloride?

MR. BOMBARITO: No, we haven't taken any ourselves. The University of North Carolina has taken some. What we have is a program with the rubber companies and we have employed the two universities--Harvard University and North Carolina--and they have been doing some studies on this.

MR. KLEIN: Do you have any results from those studies at this time?

MR. BOMBARITO: I don't.

MR. ERLICZKY: Could I respond to that? At the request of the National Institute of Occupational Safety and Health, through the offices of Dr. Joseph Waggoner, with a request to the companies that we have organized, with

whom we have contracts, we have provided whatever available epidemiological data we have for his evaluation and study. And this data has also been given to Dr. Lloyd. To date we have not seen the results of the total studies as such. We are aware that at least one of our people in one of our plants has died of angiosarcoma.

MR. KLEIN: Do you intend to submit the results of those tests either during this hearing or as post-hearing comment?

MR. EBLICZKY: We have made no attempt to do this. There is a possibility that some of the information that has been gleaned from death certificate data may be presented and referred to by Dr. John Peters and Reese Johnson.

MR. KLEIN: Now, directing your attention to technical feasibility, have you done any surveys or study with respect to technical feasibility?

MR. EBLICZKY: Would you please qualify your question on technical feasibility? It is a very technical question.

MR. KLEIN: It is my understanding that one of the issues that is going to appear at this hearing is whether or not it is technically possible to achieve one part per million. And I was wondering whether you gentlemen or any of the organizations have had the opportunity to conduct studies or things along those lines?

MR. BELICZKY: I would like to comment on that. We haven't conducted studies as such. When we talk about technical feasibilities of engineering control, we have to consider three specitic areas. Number one, the manufacture of the vinyl chloride itself. I see no great problem, from the standpoint of engineering control, to reduce the level to the least detectable amount. I don't use numbers, I am referring to Dr. Key's recommendations for air concentrations.

It is obviously much more difficult when we talk about the manufacture of homopolymer or copolymer, concentrations which we encounter in cleaning of reactor vessels, extremely high concentrations which we encounter during leak situations and blow-off situations, reactor vessels. Obviously ventilation control is a difficult one, but when we respond to that particular thing, until we introduce new techniques, such as some of our companies are currently considering, the use of tetrahydrofluoride (?) to clean reactor vessels, to minimize worker exposure to higher concentrations, obviously one must go the route of a supply type respirator.

When it comes to the manufacturing processes--and this is a situation in which sometimes I figure that a lot of the people who are quoting numbers such as 1.6 million people and two million people out of work--I think maybe

they refer primarily to the people who use the PVC resin to make a product, because there are only 7,000 people exposed to the vinyl chloride from the manufacture of the VC or the PVC resin.

I don't see a single difficult problem in initiating ventilation control in the areas where the PVC resin is used to make a product, and I have seen the majority of them. It is simple straight industrial hygiene ventilation. It is not that expensive.

And I think Mr. Bommarito quoted Mort Corn who says essentially the same thing.

It is quite difficult for me to make an evaluation of technical feasibility from the standpoint of cost--I am not involved with cost. From the standpoint of the technical feasibility, I see no difficulty in two areas and some difficulty in the manufacture of the polymer.

MR. KLEIN: Directing your attention to the cleaning, the chemical for the cleaning of the respirators, can you tell us about that, please, or would you know about it?

MR. BELICZKY: Cleaning of respirators?

MR. KLEIN: Excuse me, reactors.

MR. BELICZKY: Certainly I can tell you something about that. There are a couple of companies--I know the Uniroyal Corporation in Painesville, Ohio, had initially attempted four or five years ago--and I may not be correct

on that date--to do a better job and eliminate the high concentration of vinyl chloride to which the workers were exposed, but they would dissolve the caked PVC resin that was on the side of the reactors with a solvent called tetrahydrofluoride (?), commonly referred to as THF.

I guess their experience was not the best in the world for a couple of reasons, one being difficulty in redistilling the material; secondly, there is a hazard involved, it forms some peroxides which are hazardous, and one must consider those; third, at the time some of them used it, it didn't do the job as they had anticipated. There are certain reactor vessels in which the cooling coils are located inside the reactor vessel, and even solvent cleaning doesn't get them clean.

One of our plants that we have organized in Ashtabula, Ohio, is probably now strongly experimenting with THF as a reactor cleaner.

Robin Tech Shinitsu (?)--and I spoke to some of the Japanese rubber workers two days ago in Akron--Robin Tech has a plant in Painesville, Ohio. They are going to build some large reactors somewhere in this country which will probably be 30,000-gallon reactor vessels---and their current thinking is that they will utilize a solvent cleaning procedure, primarily THF.

I would like to caution those who are considering

the use of that solvent. We don't know as much about the toxicity of THF as we would like to know. It is combustible and I think it may again create a problem of which we have no awareness.

I think solvent cleaning is a good possibility of one way of eliminating high concentration exposures.

MR. KLEIN: I take it, then, that with the use of THF, you would not have to put an employee inside the reactor, or would an employee still have to go inside the reactor?

MR. BELICZKY: If it is done properly and the reactor vessels are designed properly, you can eliminate an employee going inside the reactor vessel. I would say that if it doesn't do the job perfectly, he would have to periodically go into the reactor vessel, but it would reduce the number of times he would have to go in to chip out a reactor.

MR. KLEIN: Directing your attention to maintenance, do you see that as a problem with respect to getting down to the one level, the 1-ppm level?

MR. BELICZKY: What do you mean by maintenance?

MR. KLEIN: Repair and maintenance.

MR. BELICZKY: Are you talking about maintenance workers?

MR. KLEIN: Well, let me give you a hypothetical,

per million, maybe if it is down to 100 parts per million or less, maybe we will have no detectable level of vinyl chloride in plants that use the product, the polymer, to make a product.

MR. KLEIN: Do you have any recommendations as to how you can reduce the unreacted monomer?

MR. BELICZKY: The unreacted monomer--I think that is a question I would have difficulty answering. I have spoken to some of the plant engineers and I have an indication that it is possible. You can reduce it by increasing vacuum and vacuum time. There may be other methods of doing it. I am not a plant engineer nor am I involved in the production of this material, but I think if I had time I could come up with some kind of an answer, if I spoke to the right people.

MR. KLEIN: Now, in the testimony, you indicated that one of the B. F. Goodrich plants had a process comparable to the French process.

Do you know which plant that is?

MR. BELICZKY: Yes, Pedrickstown, if I am not mistaken. Is that right?

MR. KLEIN: I would like to direct your attention to page 25 of the testimony. You have indicated that some of the current systems become useless when PVC resin dust is drawn into the sampling probes.

would you have some type of a time delay?

MR. BELICZKY: Which general recommendation?

MR. KLEIN: The recommendation that one part per million be set as the limit or that no detectable level be set?

MR. BOMBARITO: Well, I don't think you can put it in immediately. I think there are a number of things that the companies ought to be given an opportunity to correct. I know that in discussing with one company they had six plants that they worked at and they were bringing the concentration lower. And I am sure that somewhere in this testimony--I know he is going to appear on the program, that is Mr. Batoni from the B. F. Goodrich--explaining some of the things to get that parts-per-million down. I know that he had given us some figures and I am sure that he will produce them. He has probably done a little bit more since the last time we met which was about several months ago.

MR. KLEIN: Do you have any specific recommendations with respect to time frame?

MR. BELICZKY: I would like to make one comment. We made a plea to the Assistant Secretary of Labor that he change the current emergency temporary standard's ceiling limitation of 50 parts per million to that recommended by the IUD committee, which was less than detectable.

If the emergency temporary standard were modified and became effective tomorrow, then it would be tomorrow that

resin to make a product?

MR. KLEIN: Okay, I will be very explicit. I am talking about from the stage, from VC monomer to polymerization, compounding and fabrication, which may include extrusion and the like--through those stages, are you aware of any circumstances under which PVC would not be capable of releasing the monomer?

MR. BELICZKY: I am not aware of anything like that.

MR. KLEIN: Thank you very much, gentlemen.

JUDGE MYATT: All right, questions from the floor.

VOICE: Would you ask Mr. Beliczky to provide the data on the fibrosis of the lungs ---

JUDGE MYATT: Why don't you go to the microphone and ask.

VOICE: I don't have any question of Mr. Beliczky, I am just asking if he could provide for the record the 16 documented cases of fibrosis of the lungs, and the file on the one individual who had died in the fabricating plant.

MR. BELICZKY: I think the information on the fibrosis cases came from Dr. Selikoff and Dr. Anderson, and I think that can be made available through them. And the documentation on the one individual who died--when? The letter I read? We haven't even investigated that one yet.

[Laughter]

STATEMENT OF EARLE F. WEBSTER, TECHNICAL SUPERINTENDENT AND ASSISTANT TO THE VICE PRESIDENT OF OPERATIONS, UNILOK BELTING DIVISION OF THE GEORGIA DUCK & CORDAGE MILL, SCOTTDALE, GEORGIA; ACCOMPANIED BY HAROLD F. JONES, VICE PRESIDENT FOR MANUFACTURING, SCANDURA COMPANY; AND HARRY J. LAMBETH, COUNSEL, FIRM OF KOTHE, EAGLETON, BARTON & LAMBETH, WASHINGTON, D.C.

MR. WEBSTER: Thank you, your honor, gentlemen of the Department of Labor, my name is Earle Webster, and I am speaking on behalf of Mr. Vitek, who has been scheduled.

I am the Technical Superintendent and Assistant to the Vice President of operations of the Unilok Belting Division of the Georgia Duck & Cordage Mill of Scottdale, Georgia, a neighboring community of Atlanta. I am representing the Poly Vinyl Chloride Belting Manufacturers Committee which has a great interest in the proposed standards for occupational exposure to vinyl chloride being established by the Occupational Safety and Health Administration. I am a chemical engineer, a graduate of Yale University, and I have been involved in mechanical goods manufacturing and research and development for 30 years. In recent years I have worked with all types of elastomers, such as vinyl,

rubber, silicone, and urethane.

The PVC Belting Manufacturers Committee is comprised of five manufacturing firms who are processors of poly-vinyl chloride resin in making PVC finished conveyor belting.

I am accompanied today by Harold F. Jones, a textile engineer and Vice President for Manufacturing of the Scandura Company, Charlotte, North Carolina and our counsel, Harry J. Lambeth, of the Washington law firm of Kothe, Eagleton, Barton & Lambeth.

We want to comment on the economic and technical aspect of conforming to the proposed standard. We do appreciate and support the efforts of the Department of Labor to provide adequate safety for occupations. We join in the continued awareness of occupational hazards. Our employees are our most valued asset. We want to provide for their safety and good health in every needed manner. In the constant furtherance of our employees' wellbeing, we would not wish to see their jobs eliminated because of a standard formed as the result of over-reaction and inadequate and inconclusive information.

We want to assure you that in the event a standard is set for the manufacturer of vinyl chloride and for the conversion of vinyl chloride into polyvinyl chloride resin to which those manufacturers could not conform, there would

be a serious economic disaster brought about in our national economy. You, possibly more than we, since the issuance of the "no detectable" proposed standard, have become aware of the potential seriousness of this economic impact.

Should PVC resin become less available than it is now or none available a substantial portion of conveyor belting could not be furnished to many industries. We would comment on three major industries that use PVC conveyor belting.

1. About 30 percent of the underground coal mining belting is made from PVC resin.

2. About 50 percent of the grain handling belting is made from PVC resin.

3. About 75 percent of the sugar, meat, poultry, fish, citrus fruits, vegetables, and many other similarly processed food sources is conveyed on belting made from PVC resin.

The rubber belt manufacturers would not be able to supply the needed belting should PVC resin be unavailable to make the PVC resin belting used in the above critical industries. At this time the rubber belt deliveries are already greatly extended as indeed are PVC resin conveyor belt deliveries in areas such as for mining coal.

There is no known economically and technically

feasible substitute for PVC resin for the manufacture of the presently made PVC resin conveyor belting. We urge you in setting a permanent standard for the manufacture and polymerization of vinyl chloride, that you temper your decision for the potential economic disaster that the non-availability of PVC resin would cause.

To adequately convey our technical position about the proposed "no detectable" standard, we believe a short description of our manufacturing operations is appropriate. Thereafter, we would comment about the manner in which the presence of gas and dust is handled. Finally we would present data that we have obtained about the concentration of vinyl chloride in the atmosphere at the several points in the manufacturing operations and complete this presentation with a recommendation.

Our manufacturing operations have in part or wholly the following steps:

1. Prepare textile yarns.

2. Weave textile yarns into fabric.

3. Prepare a polyvinyl chloride plastisol which is a mixture, known as a dispersion, of polyvinyl chloride resin and plasticizer, an oily liquid, and also other powderous and liquid chemicals.

4. Saturate and overcoat the fabric with the PVC plastisol.

Prevalence of disease among
vinyl chloride and polyvinyl chloride workers

Ex 154

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by

Ruth Lilis, M.D., Henry Anderson, M.D., William J. Nicholson, Ph.D.,
Susan Daum, M.D., Alf S. Fischbein, M.D. and Irving J. Selikoff, M.D.

The emergence in January 1974, of vinyl chloride as a new occupational carcinogen, producing hemangiosarcoma of the liver, focused new and much greater attention on the toxicologic effects of this chlorinated hydrocarbon.

A considerable number of studies had been published on the rather puzzling and unique syndrome of "acroosteolysis" (Table 1) mainly describing the bone lesions in the distal phalanges of the fingers, but also the associated scleroderma-like skin lesions and the striking vascular (arterial and arteriolar) changes, pathologically the main lesion, leading to secondary bone and skin changes (Tables 2 and 3).

Much less attention had been given to the hepatotoxic effects of vinyl chloride, although convincing experimental evidence had been produced (Torkelson et al., 1961) and scattered reports of ill-defined liver changes were reported in some studies of vinyl chloride exposed workers (Table 4).

There was evidence that liver damage occurred in workers exposed to higher levels of vinyl chloride. In some studies the liver changes (hepatomegaly, tenderness on palpation, abnormal liver tests) were found to be reversible after cessation of exposure. On the other hand, some observations mentioned the progressive nature of the liver changes, when toxic exposure continued, to what was stated to be "chronic hepatitis".

Recent work from Germany (Marsteller et al., 1973) reporting a detailed study of 20 PVC workers, brought a very important contribution to our present knowledge on the liver changes induced by this toxic exposure. The authors were alerted to the problem by the occurrence of upper gastrointestinal bleeding in several workers of a PVC producing plant. Esophageal varices, splenomegaly, hepatomegaly, fibrosis of the liver capsule (by laparoscopy), delay in the excretion of bromsulphalein, thrombocytopenia, were the most prominent findings. The pathological changes encompassed collagenous transformation of the liver sinusoids, focal activation of Kupffer cells, increased collagen deposition in the portal spaces, portal fibrosis, septal and intralobular fibrosis.

There were a few reports in the literature of lung changes in PVC workers. One case of pneumoconiosis in a thirty year old worker who had inhaled PVC dust was reported. The lung biopsy showed granulomatous lesions (foreign body type) to be present. Fibrotic changes and altered pulmonary function tests were reported in 96 workers exposed to polyvinyl chloride dust; the changes were more pronounced in persons with long exposure (Verkin et al. 1970).

This study was supported by research grant ES 00023 of the National Institute of Environmental Health Sciences, Department of Health, Education and Welfare.

In the available literature on vinyl chloride and polyvinyl chloride adverse health effects there were no accurate data on the prevalence of disease in exposed workers, the relative prolevence of the various pathologic changes, their possible association and time sequence.

We have undertaken clinical studies of a number of groups of vinyl chloride exposed workers in order to assess the prevalence of vinyl chloride induced changes and to define the natural history of this occupational disease. We are reporting the results of a survey (March 1974) of 267 workers currently employed in a VC polymerization plant, including virtually the entire current production workforce. 87 former workers were examined as well. In both groups, exposure for some had started in 1946, when the plant opened. Altogether 354 men were examined.

Table 5 shows the duration of exposure for the group and Table 6 the age distribution of the men. More than half were under 40 years, 20% were 51 or older.

METHODS

The medical examination included detailed occupational history, past medical history, physical examination with special attention to the skin, hands and feet, arteries accessible to palpation, liver and spleen.

An Allen test for the assessment of the peripheral circulation in the areas supplied by the radial and ulnar arteries was performed. Each examined worker also had the following:

> X-rays of the chest, hands and feet; pulmonary function tests; complete blood cell counts including platelets; blood chemistries including bilirubin, SGOT, SGPT, LDH, alkaline phosphatase, total protein, electrophoresis of serum proteins, fibrinogen split products; alpha fetoprotein, antinuclear antibodies, antimitrochondrial antibodies, antismooth muscle antibodies Australia antigen B by radioimmunoassay and liver antibodies. Urinalysis, including microscopic examination of the sediment, was done. All examined workers were also tested for carcinogenic embryonic antigen. In a limited number, studies for chromosome breaks in circulating lymphocytes were undertaken.

RESULTS

Unfortunately, appropriate VC measurements had not been made in the past. We have findings which suggest, however (Table 7), that VC levels may have been considerable at times, sufficient to produce symptoms of acute overexposure; for example, 14 of the 354 workers had had loss of consciousness at one time or another.

In any case, our data indicate that measured levels would be of limited utility, unless integrated over time, since both total exposure and duration from onset of exposure seem to be of importance in relation to likelihood of abnormality. The influence of these variables may be demonstrated in a number of ways.

This was so insofar as abnormal peripheral circulation was concerned (Table 8).

Numbness and tingling of the fingers, along with increased sensitivity to cold, were early symptoms. They were often associated with pain and cyanotic discoloration sometimes also involving the toes. Classical Raynaud's syndrome, characterized by cold-induced, marked, sudden and sharply demarcated pallor of the fingers followed by cyanotic discoloration in the same area, was only found in 5.6% of the cases. In general, the effect of vinyl chloride exposure on the peripheral vessels of hands and feet appears to produce a wider range of symptoms than those characteristic of Raynaud's syndrome.

As noted, the prevalence of these changes rose with duration of exposure. Typical Raynaud's syndrome was found in almost 10% of cases with more than 20 years of exposure. The prevalence of Raynaud's syndrome was significantly higher in workers with more than 10 years of exposure, than in those with less than 10 years exposure. Symptoms of abnormal peripheral circulation (Table 9) were more frequent in workers currently exposed than in those with past exposure.

An abnormal Allen test indicating delayed arterial circulation in the areas supplied by the ulnar and/or radial arteries, was found in 94 (26.6%) of the examined workers (Table 10).

The percentage of persons with abnormal Allen tests increased with their length of exposure. The prevalence of an abnormal Allen test in workers with more than 5 years exposure was significantly higher than in those with less than 5 years exposure.

Pseudo-clubbing of the fingers was also found with increasing frequency as the duration of employment increased; the overall prevalence was 8.7%; in the group with more than 20 years of exposure it was 17.3% (Table 11). However the difference in the prevalence of pseudo-clubbing between workers with less and more than 5 years of exposure did not quite reach the level of statistical significance. ($X^2 = 3.692$) Pseudo-clubbing was almost always associated with signs and/or symptoms of abnormal peripheral circulation, and was a more frequent finding that typical Raynaud's syndrome. In some cases, especially in persons with past exposure, there was a history of Raynaud's syndrome which had gradually faded, while pseudo-clubbing had persisted or even progressed.

Skin changes (Table 12) involving the fingers, hands, forearms and sometimes face, were found in 23 examined workers. The fingers and hands appeared to be slightly edematous, the skin was thickened, tense and stiff, with decreased elasticity and sparse folding. Well circumscribed plaque or band areas of scleroderma-like skin changes, as described by others, were not found. In 9 of the 23 cases in which skin changes were found, Raynaud's syndrome was also present.

Pain in the small joints of the fingers and hands (Table 13), was a complaint in 28 (8%) of cases and was found mainly in workers with current exposure, even of short duration (Table 14). There was no special trend regarding pain in other joints, except for the wrists, where most of the cases were found in workers with more than 5 years of exposure. There were no symptoms suggesting involvement of the sacroiliac joints, and no radiologic evaluation was undertaken.

Bone changes in the distal phalanges of fingers and toes will be separately reported in detail. While slight changes, such as marginal cortical defects and slight tuft resorbtion were not uncommon, transverse defects and fractures were found in only 4 cases.

We were interested in the possibility that hypertension (Table 15) might be of importance. We did not find this to be so. The overall prevalence of hypertension (as defined by WHO criteria) was 12%. There was no correlation with peripheral vascular impairment in the hands and feet. Abnormal urinary findings were not prominent either (Table 16).

The liver was found to be slightly or moderately enlarged in 15% of the cases (1 to 2 finger breadth below the right costal margin; 11 to 13cm vertical span (Table 17); this finding was more frequent in workers with longer duration of exposure. Only in one case was the liver found to be markedly enlarged. The inferior pole of the spleen was palpable in 12 (3.4%) of cases: Again, only one person had marked splenomegaly. There was a highly significant difference in the prevalence of enlarged liver in workers with more than 5 years exposure as compared with those with shorter exposure. The same comparison for splenomegaly did not show a statistically significant difference. According to the past medical history, a diagnosis of cirrhosis of the liver had been made previously in 5 cases. Esophageal varices had been diagnosed in one patient who had undergone surgery, including portocaval shunt, 12 years before the present examination, with good clinical result.

Abnormal liver function tests (Table 18) were found in small percentages (6% for bilirubin and SGOT, 9% for SGPT), except for alkaline phosphatase which was elevated in 59 (16.6%) of cases).

Duration of exposure correlated with an increase in the prevalence of elevated alkaline phosphatase, especially in workers with more than 5 years of exposure.

There was a higher percentage of abnormal liver tests in workers with current exposure than in those with past exposure (Table 19). Alkaline phosphatase was an exception, since similar proportions of abnormal tests were found in persons with current or prior exposure.

The best correlation between clinical findings of hepatomegaly and/or splenomegaly and abnormal liver function tests was found to be that with elevated alkaline phosphatase (Table 20); 41% of those with such clinical abnormalities had increased alkaline phosphatase.

Hematologic abnormalities were scant in our study. Thrombocytopenia, a frequent finding in the German studies, was present in only one of the examined workers (Table 21).

The possible contributory effect of significant ethanol intake was carefully considered (Table 22): no trend as related to duration of exposure could be found for ethanol intake.

In one-third of the cases with clinical liver and/or spleen changes significant ethanol intake could have been a factor (Table 23), and in 25% of the cases with increased alkaline phosphatase was there a history of significant intake (Table 24). Further, the prevalence of an enlarged

liver and/or spleen in persons with and without significant ethanol intake was compared (Table 25). While there was no statistically significant difference in workers with less than 10 years of exposure, in those with more than 10 years exposure, there was a higher prevalence of enlarged liver and/or spleen in persons with a significant ethanol intake. A multiple factor additive interaction may be considered.

Liver function tests were also analyzed in relation to ethanol intake (Table 26). There was no significantly higher prevalence of elevated alkaline phosphatase, bilirubin or LDH in the group with significant ethanol intake. However, high SGOT or SGPT values were notably more frequent in this group. It is of interest that elevated alkaline phosphatase, the most frequent biochemical abnormality found, did not correlate with ethanol intake, while there was a significant correlation with duration of vinyl chloride exposure.

Many of the examined workers (Table 27) gave a past medical history of "gastritis," ulcer (gastric and duodenal), upper gastrointestinal bleeding (most often attributed to ulcer) and gallbladder disease. However, it is difficult to know whether such symptoms were more common than might be expected in a similar group without VC exposure.

Out of the 115 workers with such past medical history, there were 28 (25%) who were found to have enlarged liver and/or spleen (Table 28); the percentage was 38% for those with past upper gastrointestinal bleeding and 33.4% for those with a history of gallbladder disease. In the other 242 workers without such a past medical history, 29 (12%) were found to have an enlarged liver and/or spleen.

Chest x-rays of 142 examined workers were available at the time that this report was prepared. In some of the cases linear reticular and less often nodular changes were found in the middle and lower lung fields (Table 29). No relationship was observed with smoking or chronic bronchitis (Tables 30 and 31). The significance of these changes is difficult to evaluate at this point since most of the workers had been exposed to particulate polyvinyl chloride resin as well as to vinyl chloride. Three of those with abnormal chest x-ray findings had had previous dust exposure (in coal mines for periods ranging from 4 to 9 years). There was no relationship between chest x-ray changes and liver changes, but signs and symptoms of peripheral vascular impairment (Raynaud's syndrome, cyanosis, pseudoclubbing, positive Allen test) (Table 32) were found in more than half (58%) of cases with abnormal chest x-ray findings. The prevalence of Raynaud's syndrome was significantly higher in the group with abnormal chest x-rays.

## Discussion and Conclusions

Our findings confirm the broad outlines of the clinical syndromes reported by other investigators.

In the examined group relatively high VC exposure had occurred in the past, and symptoms of acute prenarcotic effects were reported by more than half of the examined workers.

Clinical signs and symptoms of abnormal peripheral circulation in the fingers and toes were quite frequent, with cyanosis present in 13 percent, excessive sensitivity to cold in 18 percent and numbness and tingling of the fingers in 24 percent of cases. A typical Raynaud's syndrome was present in 5.7% of cases. An abnormal Allen test, indicating delayed arterial circulation in the areas supplied by the ulnar and/or radial arteries was found in 91 (26.6%) of the examined workers. The prevalence of all these abnormalities increased with length of VC exposure.

Hepatomegaly was a finding in 13% of the examined workers, while splenomegaly was found in 3.4%. Cirrhosis of the liver had been previously diagnosed in 5 workers, and, in one, esophageal varices with upper gastrointestinal bleeding had led to surgery including portocaval shunt.

Alkaline phosphatase was the test which was most frequently found to be abnormal and showed the best correlation with clinical findings.

Hepatomegaly and elevated alkaline phosphatase were significantly more frequent in workers with longer VC exposure.

Radiologic pulmonary changes, linear reticular and nodular opacities in the lower and middle lung fields were found in a number of cases; the prevalence of these changes was higher with longer duration of exposure, and there was a significant association with peripheral circulation abnormalities. The evaluation of these pulmonary changes is still in progress.

Our results indicate that liver involvement and probably lung involvement in PVC workers are significant and should be given full attention in the medical surveillance of workers with past exposure.

Future exposure to vinyl chloride should be controlled in order to prevent development of all adverse effects, including the carcinogenic effect.

Table 1

Acroosteolysis

| | | |
|---|---|---|
| 1957 | Filatova and Greenberg | "Angioneurosi.. of spastic character" |
| 1963 | Suciu et al | - Raynaud's syndrome - (hands and feet) 6% of 168 exposed workers<br>- Scleroderma-like skin changes - (hands feet, face, neck, thorax) 3.6% of examined |
| 1966 | Cordier | - Raynaud's syndrome<br>- Scleroderma-like skin changes<br>- Lytic lesions of terminal phalanges in hands and feet |
| 1967 | Harris and Adams | - The same changes and - pseudoclubbing of fingers<br>- Involvement of sacro-iliac joints and patella |
| 1967 | Wilson et al | - |
| 1971 | Dinman et al | |
| 1972 | Markowitz et al | Skin biopsy and pathology data |
| 1972 | Jühe et al | Arteriography<br>Occlusion of interosseous arteries |
| 1973 | Misgeld et al | Arteriography —> spastic arteries visualized only after Priscol |

Table 2

Acroosteolysis

Bone Changes

- Marginal and/or cortical defects in distal phalanges
- Loss of cortex in tufts of the distal phalanges
- "Half-moon" defects or cuts
- Transverse defects or fractures
- Complete resorption of tufts and part of shafts
- Involvement of the larger bones
  Cystic lesions and increased radiolucency
  (ulna, radius, humerus, os calcis, patella)
- Erosive and sclerotic changes in sacro-iliac joints

Table 3

Acroosteolysis

Skin biopsy pathology

- Thickening of dermis
- Nonfibrillary homogenization of collagen and thickened collagen bundles
- Disorganization of elastic fibers, which are split and broken
- Inflammatory infiltrates, predominantly perivascular (lymphocytes, few histiocytes)
- Thickening of the media of dermal arterioles
- Uneven endothelial thickening
- Marked swelling of dermal nerve fibers vacuolization of axones
- Intersititial edema
- Dilatation of lymphatics

Table 4

Evidence of liver damage in PVC exposed workers

| | | |
|---|---|---|
| 1949 | "Hepatitis-like liver changes" | Tribuch et al. (USSR) |
| 1963 | "Chronic epithelial hepatitis" in 15% of cases; hepatomegaly, increased bilirubin and prothrombin time, abnormal Takata-Ara test. | Pushin (USSR) |
| 1963 | Hepatomegaly in 30% of 168 examined workers, splenomegaly (6%). Liver biopsy in 2 cases: "chronic hepatitis." | Suciu et al (Romania) |
| 1967 | Hepatomegaly; persistent raised bilirubin. | Harris (England) |
| 1967 | Increased BSP retention, raised icterus index———related to degree of exposure. | |
| 1972 | Pain in RUQ and abnormal liver tests (in 2 out of 7 patients with scleroderma-like skin changes). | Jühe et al (Germany) |
| 1973 | RUQ discomfort; abnormal liver changes. | Misgeld et al (Germany) |

Table 5

Duration of vinyl chloride exposure among 354 workers in Niagara Falls

| Duration of exposure (years) | Currently employed | Formerly employed | Total |
|---|---|---|---|
| ≤ 2 | 36 | 25 | 61 |
| 2.1–5 | 62 | 13 | 74 |
| 5.1–10 | 47 | 15 | 62 |
| 10.1–20 | 77 | 27 | 104 |
| 20+ | 45 | 7 | 52 |
| | 267 | 87 | 354 |

Table 6

Age distribution of 354 vinyl chloride exposed workers (Niagara Falls)

| Duration of exposure (years) | Age groups (years) | | | | | Total |
|---|---|---|---|---|---|---|
| | 21-30 | 31-40 | 41-50 | 51-60 | 60+ | |
| ≤ 2 | 39 | 9 | 8 | 4 | 1 | 61 |
| 2.1-5 | 45 | 17 | 9 | 1 | 3 | 75 |
| 5.1-10 | 17 | 18 | 24 | 3 | 0 | 62 |
| 10.1-20 | 0 | 50 | 30 | 21 | 3 | 104 |
| 20+ | 0 | 4 | 14 | 27 | 7 | 52 |
| Total | 101 | 98 | 85 | 56 | 14 | 354 |

Table 7

Symptoms of acute overexposure
among 354 vinyl chloride workers

| Duration of Exposure (years) | Number of examined workers | Symptoms | | | | Total | % |
|---|---|---|---|---|---|---|---|
| | | Headache | Light-headedness | Dizziness | Loss of Consciousness | | |
| < 2 | 61 | 12 | 21 | 0 | 3 | 28 | 46 |
| 2.1-5 | 75 | 13 | 30 | 30 | 3 | 43 | 57 |
| 5.1-10 | 62 | 8 | 23 | 20 | 0 | 33 | 53 |
| 10.1-20 | 104 | 17 | 40 | 44 | 7 | 56 | 53 |
| 20+ | 52 | 7 | 26 | 32 | 1 | 36 | 69 |
| Total | 354 | 57 (16%) | 142 (40%) | 135 (38%) | 14 (4%) | 196 | 55% |

Table 3

Clinical signs and symptoms of abnormal peripheral circulation among 354 vinyl chloride exposed workers

| Duration of Exposure (years) | Total Number | Numbness Tingling | | Excessive Sensitivity to cold | | Pain | | Cyanosis | | Involvement of toes | | Raynaud's* syndrome | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| ≤ 2 | 61 | 2 | (3%) | 2 | (3%) | | | 2 | (3%) | | | | |
| 2.1-5 | 75 | 16 | (21%) | 11 | (15%) | 4 | (5%) | 4 | (5%) | 1 | (1%) | 2 | (2.6%) |
| 5.1-10 | 62 | 11 | (18%) | 11 | (18%) | 3 | (5%) | 10 | (16%) | 5 | (8%) | 4 | (6.4%) |
| 10.1-20 | 104 | 36 | (35%) | 26 | (25%) | 11 | (11%) | 19 | (18%) | 11 | (11%) | 9 | (8.6%) |
| 20.1 | 52 | 20 | (38%) | 13 | (19%) | 10 | (19%) | 11 | (21%) | 8 | (15%) | 3 | (5.8%) |
| Total | 354 | 85 | (24%) | 63 | (18%) | 28 | (8%) | 46 | (13%) | 25 | (7%) | 20 | (5.7%) |

*Prevalence in workers with more than 10 years exposure significantly higher than in those with less than 10 years exposure.

$\chi^2 = 5.783$

$p < 0.02$

Table 9

Raynaud's Syndrome among 354 vinyl chloride workers

| Exposure | Number | Raynaud's Number | Raynaud's % |
|---|---|---|---|
| Active | 267 | 17 | 6.4 |
| Prior | 87 | 3 | 3.4 |
| | 354 | 20 | 5.6 |

Abnormal Allen Test among
354 vinyl chloride workers

| Duration of Exposure (years) | Abnormal Test Results | | Total* |
|---|---|---|---|
| | Current Exposure | Prior Exposure | |
| ≤ 2 | 7/36 | 2/25 | 9/61 (14.7%) |
| 2.1-5 | 11/62 | 7/13 | 18/75 (24.0%) |
| 5.1-10 | 16/47 | 7/15 | 23/62 (37.1%) |
| 10.1-20 | 22/77 | 5/27 | 27/104(26.0%) |
| 20+ | 12/45 | 5/7 | 17/32 (32.7%) |
| | 68/267(25.5%) | 26/87(29.9%) | 94/354(26.6%) |

Radial - 10
Ulnar - 38
Both - 46

*Prevalence of abnormal Allen Test in workers with more than 5 years exposure significantly higher than in those with less than 5 years exposure. $\chi^2 = 5.084$

$0.02 < p < 0.05$

Table II

Pseudo-clubbing of fingers among 354 vinyl chloride workers

| Duration of exposure (years) | Pseudo-clubbing of fingers: Current exposure | Past exposure | Total |
|---|---|---|---|
| ≤ 2 | 2/36 | 2/25 | 4/61 (6.5%) |
| 2.1-5 | 3/62 | 0/13 | 3/75 (4.0%) |
| 5.1-10 | 3/47 | 3/15 | 6/62 (9.7%) |
| 10.1-20 | 7/77 | 2/27 | 9/104 (8.6%) |
| 20+ | 7/45 | 2/7 | 9/52 (17.3%) |
| | | | 31/354 (8.75%) |

In 25 cases - signs/symptoms of peripheral vascular disease.

In 8 cases - typical Raynaud's syndrome.

Table 12

Skin changes in 354
vinyl chloride exposed workers

| Duration of exposure (years) | Total number examined | Skin changes | |
|---|---|---|---|
| | | Number | % |
| ≤ 2 | 61 | 4 | 6.5 |
| 2.1–5 | 75 | 2 | 2.6 |
| 5.1–10 | 62 | 3 | 4.8 |
| 10.1–20 | 104 | 8 | 7.7 |
| 20+ | 52 | 6 | 11.5 |
| Total | 354 | 23 | 6.4 |

Raynaud's syndrome was present in 9 cases.

Table 13

Pain in joints of fingers and hands

| Duration of exposure (years) | Total number examined | Fingers, Hands | | Wrists | |
|---|---|---|---|---|---|
| | | No. | % | No. | % |
| ≤ 2 | 61 | 5 | 8.1 | 1 | 1.6 |
| 2.1-5 | 75 | 5 | 6.7 | | |
| 5.1-10 | 62 | 2 | 3.2 | 1 | 1.6 |
| 10.1-20 | 104 | 8 | 7.7 | 3 | 2.9 |
| 20+ | 52 | 8 | 15.4 | 1 | 2.0 |
| Total | 354 | 28 | 8.0 | 6 | 1.7 |

Note: Difference in prevalence not significant for workers with less than 10 years or more than 10 years of exposure.

Table 14

Pain in the joints of fingers and hands

| | Total number examined | Pain in finger and hand joints | |
|---|---|---|---|
| | | No. | % |
| Current exposure | 267 | 24 | 9.0 |
| Past exposure | 87 | 4 | 4.6 |
| Total | 354 | 28 | 8.0 |

Table 15

Hypertension among 354 vinyl chloride workers

| Duration of exposure (years) | Exposure | Hypertension: Systolic | Diastolic | Systolic and Diastolic | Total |
|---|---|---|---|---|---|
| ≤ 2 | 36 Current | 0 | 0 | 2 | 2 |
| | 25 Prior | 0 | 1 | 2 | 3 |
| 2.1-5 | 62 Current | 1 | 0 | 2 | 3 |
| | 13 Prior | 1 | 0 | 0 | 1 |
| 5.1-10 | 47 Current | 1 | 0 | 2 | 3 |
| | 15 Prior | 0 | 1 | 1 | 2 |
| 10.1-20 | 77 Current | 3 | 2 | 4 | 9 |
| | 27 Prior | 3 | 1 | 2 | 6 |
| 20+ | 45 Current | 3 | 5 | 4 | 12 |
| | 7 Prior | 0 | 0 | 2 | 2 |
| Total | 354 | 12 | 10 | 21 | 43 (12%) |

Note: Workers with hypertension had no greater prevalence of peripheral vascular changes in hands and feet.

Elevated BUN present in only three instances.

Table 16

Abnormal urine findings among 354 vinyl chloride workers

| Duration of exposure (years) | Current exposure | Protein 1+ | RBC | Casts |
|---|---|---|---|---|
| ≤ 2 | 36 Current | 1 | 0 | 2 |
| | 23 Prior | 2 | 0 | 0 |
| 2.1-5 | 62 Current | 2 | 0 | 2 |
| | 13 Prior | 1 | 0 | 0 |
| 5.1-10 | 47 Current | 1 | 1 | 1 |
| | 15 Prior | 0 | 1 | 0 |
| 10.1-20 | 77 Current | 1 | 6 | 0 |
| | 27 Prior | 1 | 1 | 1 |
| 20+ | 45 Current | 1 | 3 | 0 |
| | 7 Prior | 0 | 0 | 0 |
| | 354 | 10 | 12 | 6 |

Table 17

Hepatosplenomegaly among
354 vinyl chloride workers

| Duration of exposure (years) | Total number examined | Enlarged liver* | | Enlarged spleen** | |
|---|---|---|---|---|---|
| | | No. | % | No. | % |
| ≤ 2 | 61 | 4 | 6.5 | 1 | 1.6 |
| 2.1-5 | 75 | 5 | 6.7 | 2 | 2.7 |
| 5.1-10 | 62 | 7 | 11.3 | 2 | 3.2 |
| 10.1-20 | 104 | 20 | 19.0 | 3 | 2.9 |
| 20+ | 52 | 17 | 32.7 | 4 | 7.7 |
| Total | 354 | 53 | 15.0 | 12 | 3.4 |

*Difference in prevalence of enlarged liver in workers exposed for less than 5 years as compared to those exposed for more than 5 years. $\chi^2 = 12.107$, $p < 0.001$

**For enlarged spleen $\chi^2 = 0.945$, n.s.

Table 18

Abnormal LFT among 354
vinyl chloride workers

| Duration of exposure (years) | Total number examined | Bilirubin >1.1 | SGOT (>36) | SGPT >36 | LDH >225 | Alk. Phos.* >83 | |
|---|---|---|---|---|---|---|---|
| ≤ 2 | 61 | 2 | 3 | 5 | 0 | 9 | 12.9% |
| 2.1-5 | 75 | 5 | 4 | 7 | 0 | 7 | 9.3% |
| 5.1-10 | 62 | 7 | 3 | 5 | 4 | 11 | 17.7% |
| 10.1-20 | 104 | 2 | 6 | 8 | 3 | 19 | 18.2% |
| 20+ | 52 | 3 | 4 | 6 | 1 | 13 | 25.0% |
| Total | 354 | 21(6%) | 20(6%) | 31(9%) | 8(2.3%) | 59 | (16.6%) |

*Prevalence of elevated alkaline phosphatase significantly higher in workers with more than 5 years exposure than in those with less than 5 years exposure.

$\chi^2 = 3.84$ $p=0.05$

Table 19

Abnormal LFT among 354 vinyl chloride workers currently or previously employed

| Liver function test | | Current employment (267) | Prior employment (87) | Hepatosplenomegaly, Hepatic tenderness (60) |
|---|---|---|---|---|
| Bilirubin | >1.1 | 18 (6.7%) | 3 (3.6%) | --- |
| SGOT | >50 | 17 (6.4%) | 3 (3.6%) | 6/20 (30.0%) |
| SGPT | >56 | 26 (9.7%) | 5 (5.7%) | 8/31 (26.9%) |
| LDH | >225 | 6 (2.4%) | 2 (2.3%) | --- |
| Alk. Phos. | >86 | 43 (16.0%) | 16 (18.0%) | 27/59 (45.8%) |

Table 20

Relation of hepato and/or splenomegaly
to elevated alkaline phosphatase
among 354 vinyl chloride workers

| Duration of exposure (years) | No. | Enlarged liver and/or spleen, or hepatic tenderness | Elevated alkaline phosphatase | |
|---|---|---|---|---|
| ≤ 2 | 61 | 7 | 3 | 43% |
| 2.1-5 | 75 | 7 | 1 | 14% |
| 5.1-10 | 62 | 10 | 4 | 40% |
| 10.1-20 | 104 | 20 | 10 | 45% |
| 20+ | 52 | 20 | 9 | 45% |
| | 354 | 64 | 27 | 41% |

Table 21

Hematologic changes in 354 vinyl chloride workers

| | Total number examined | Thrombocytopenia <150.000 | Leucopenia <4.000 | Leucopenia 4,000-5,000 | Hemoglobin <14 gr. |
|---|---|---|---|---|---|
| 5 2 | 31 | | 1 | 8 | 1 |
| 2.1-5 | 75 | | 3 | 6 | 1 |
| 5.1-10 | 62 | | 1 | 2 | |
| 10.1-20 | 104 | | | 6 | 4+ |
| 20+ | 52 | 1 | | 6 | 2++ |
| Total | 354 | 1 (0.3%) | 5 (1.4%) | 28 (7.8%) | 8 (2.2%) |

+persons with past history of G.I. bleeding.

Table 22

Alcohol intake
in 354 vinyl chloride exposed workers

| Duration of exposure (years) | Total number examined | Alcohol Intake ++ (1-2 quarts/week) | +++ (2-3 quarts/week) | ++++ Known alcoholic | Total No. | Total % |
|---|---|---|---|---|---|---|
| 2 ≥ | 61 | 10 | 5 | 0 | 15 | 24.6 |
| 2.1-5 | 75 | 11 | 4 | 1 | 16 | 21.2 |
| 5.1-10 | 62 | 13 | 0 | 0 | 13 | 21 |
| 10.1-20 | 104 | 9 | 4 | 0 | 13 | 12.5 |
| 20.1-> | 52 | 10 | 1 | 1 | 12 | 23 |
| Total | 354 | 53 15% | 14 3.9% | 2 0.6% | 69 | 19.5% |

Table 23

## Significant alcohol intake and liver changes (clinical)

| Duration of exposure (years) | Total number examined | Enlarged liver and/or spleen or hepatic tenderness | | Cases with significant alcohol intake | |
|---|---|---|---|---|---|
| | | No. | % | No. | % |
| ≤ 2 | 61 | 7 | 11.5% | 2 | 3.3% |
| 2.1-5 | 75 | 7 | 9.4% | 3 | 4.0% |
| 5.1-10 | 62 | 10 | 16.0% | 4 | 6.5% |
| 10.1-20 | 104 | 21 | 20.0% | 4 | 3.8% |
| 20+ | 52 | 20 | 38.0% | 8 | 15.0% |
| | 354 | 65 | 18.2% | 21 | 6.2% |

Table 24

Elevated alkaline phosphatase and significant alcohol intake

| Duration of exposure (years) | Total examined | ↑ Alkaline phosphatase No. | % | Significant alcohol intake No. | % |
|---|---|---|---|---|---|
| ≤ 2 | 61 | 9 | 12.6 | 1 | 1.6 |
| 2.1-5 | 75 | 7 | 9.3 | 1 | 1.3 |
| 5.1-10 | 62 | 11 | 17.7 | 6 | 9.7 |
| 10.1-20 | 104 | 19 | 18.2 | 2 | 1.9 |
| 20+ | 52 | 13 | 25 | 4 | 7.7 |
| Total | 354 | 59 | 16 | 14 | 3.9 |

Table 25

## Hepato- and/or splenomegaly and significant alcohol intake

| | Total number examined | Significant alcohol intake | | | No significant alcohol intake | | |
|---|---|---|---|---|---|---|---|
| | | Total number | Enlarged liver and/or spleen | | Total number | Enlarged liver and/or spleen | |
| | | | No. | % | | No. | % |
| ₹ 2 | 61 | 15 | 2 | 13.4% | 46 | 7 | 15.0% |
| 2.1-5 | 75 | 16 | 2 | 12.5% | 59 | 4 | 6.8% |
| 5.1-10 | 62 | 13 | 4 | 30.8% | 49 | 5 | 10.2% |
| 10.1-20 | 104 | 13 | 4 | 30.8% | 91 | 17 | 18.7% |
| 20+ | 52 | 12 | 8 | 75.0% | 40 | 12 | 30.0% |
| Total | 334 | 69 | 20 | 29.0% | 285 | 45 | 16.0% |

Difference in prevalence of enlarged liver and/or spleen between the group with alcohol intake and those without alcohol intake non-significant for workers with less than 10 years of exposure. $\chi^2 = 1.931$ n.s.

Significant for workers with more than 10 years exposure.

$\chi^2 = 7.243$
$p < 0.01$

Table 26

Alcohol intake and abnormal liver function tests

| | Total number examined | Alkaline phosphatase | | Bilirubin | | SGOT | | SGPT | | GGT | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | No. | % | No. | % | No. | % |
| Significant alcohol intake | 69 | 14 | 20.3% | 1 | 1.4% | 9 | 13.0% | 11 | 16.0% | 2 | 2.9% |
| Non-significant alcohol intake | 285 | 45 | 15.8% | 20 | 7.0% | 11 | 3.9% | 20 | 7.6% | 6 | 2.1% |
| Total | 354 | 59 | 16.0% | 21 | 6.0% | 20 | 6.0% | 31 | 9.0% | 8 | 2.3% |
| | | $\chi^2$ = 0.810 n.s. | | $\chi^2$ = 3.087 n.s. | | $\chi^2$ = 8.790 p <0.01 | | $\chi^2$ = 5.337 p <0.01 | | n.s. | |

Table 27

Gastrointestinal disease (by history) in 354 vinyl chloride exposed workers

| | No. | | % | |
|---|---|---|---|---|
| "Gastritis" | 47 | | 13 | |
| Ulcer (gastric or duodenal) | 31 | 52 | 9 | 15 |
| Ulcer and upper G.I. bleeding | 21 | | 6 | |
| Gall bladder disease | 13 | | 3.6 | |
| Total | 112 | | | |

Table 28

Gastrointestinal disease (by history) and enlarged liver and/or spleen (clinical examination)

| | Total number | Enlarged liver | |
|---|---|---|---|
| | | No. | % |
| "Gastritis" | 47 | 8 | 17.0% |
| Ulcer (gastric or duodenal) | 31 | 7 | 22.6% |
| Ulcer and upper G.I. bleeding | 21 | 8 | 38.0% |
| Gall bladder disease | 13 | 5 | 38.4% |

Table 29

Chest x-ray abnormalities* among
142 vinyl chloride workers

| Duration of Exposure (years) | Current Exposure | X-Ray findings: Normal | Abnormal | |
|---|---|---|---|---|
| ≤ 2 | 13 Current | 12 | 1 | 5.2% |
| | 3 Prior | 6 | 0 | |
| 2.1-5 | 32 Current | 25 | 7 | 23.0% |
| | 3 Prior | 2 | 1 | |
| 5.1-10 | 19 Current | 18 | 1 | 11.0% |
| | 8 Prior | 6 | 2 | |
| 10.0-20 | 32 Current | 17 | 15 | 48.6% |
| | 5 Prior | 2 | 3 | |
| 20+ | 23 Current | 15 | 3 | 33.3% |
| | 1 Prior | 1 | 0 | |
| Total | 142 | 104 | 38 | 27.0% |

*Data incomplete.

Table 30

Chest x-ray and smoking

| Chest x-ray | Total number | Smokers | | Ex smokers | | Non-smokers | |
|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | No. | % |
| Normal | 104 | 53 | 51 | 23 | 22 | 28 | 27 |
| Abnormal | 38 | 25 | 66 | 6 | 16 | 7 | 18 |

Prevalence of abnormal chest x-ray in persons with history of smoking not significantly different from that in non-smokers. $\chi^2 = 1.033$ n.s.

Table 31

Chest x-ray and chronic bronchitis

| Chest x-ray | Total number | History of chronic bronchitis | | No history of chronic bronchitis | |
|---|---|---|---|---|---|
| | | No. | % | No. | % |
| Normal | 104 | 20 | 21 | 84 | 79 |
| Abnormal | 38 | 8 | 19 | 30 | 81 |

Table 32

Abnormal chest x-ray and abnormal peripheral circulation

| Chest X-Ray | | Raynaud's syndrome | | Cyanosis | | Pseudo-clubbing | | Abnormal Allen test | |
|---|---|---|---|---|---|---|---|---|---|
| | | No. | % | No. | % | No. | % | No. | % |
| Normal | 104 | 5 | 4.8 | 9 | 8.6 | 8 | 7.7 | 20 | 19 |
| Abnormal | 38 | 7 | 18.4 | 6 | 16.0 | 7 | 18.4 | 13 | 34 |
| | | $\chi^2 = 6.667$ $p < 0.01$ | | | | | | $\chi^2 = 3.501$ n.s. | |

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